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PREFACE

The scope of the work of the Chemical Laboratory of the American Medical Association has been described in previous volumes, but to prevent misapprehension it seems worth while to review its activities again here. The Laboratory was established primarily to aid the Association's Council on Pharmacy and Chemistry in determining the character and quality of the proprietary and unofficial medicaments offered to the medical profession. As a part of this duty, the Laboratory examines the various preparations which are proposed for inclusion in the Council's publication, "New and Nonofficial Remedies," and also other medicinal preparations regarding which it is deemed important that the medical profession be informed. Since its establishment in 1906, the sphere of the Laboratory's activities has constantly widened. Thus it supplies information on chemical topics to various departments of THE JOURNAL — Queries and Minor Notes and the Propaganda Department, for instance. In particular, it has devoted much time during recent years to the analysis of "patent medicines" and quack nostrums, thus furnishing material for the campaign of the Propaganda Department of THE JOURNAL in the interests of public health.

The reports of the Laboratory are published in order that its findings may be readily available to those who are interested in the composition of medicines, namely, drug analysts, food and drug authorities, pharmacists, and others. The methods of analysis, when believed to be of interest, are reported in detail in the hope that this information may be of help to those engaged in drug analysis.

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PART I

REPRINTS OF CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION

THE QUALITY OF COMMERCIAL BLAUD'S PILLS

L. E. Warren, Ph.C., B.S.

(Reprinted, with additions, from The Journal A. M. A., April 17, 1915, p. 1344

In view of the known instability of ferrous salts, it has been generally held that pills of ferrous carbonate U. S. P. (Pilulae Ferri Carbonatis, U. S. P.), commonly known as Blaud's pills, are unstable. Thus, the U. S. Pharmacopeia directs that they shall be freshly prepared when wanted. Pharmaceutic manufacturing houses, evidently holding this requirement to be unnecessary, almost universally sell ready-made Blaud's pills. On the other hand, some firms sell special forms of the preparation with claims of keeping qualities superior to the ordinary pill. Nevertheless, it was recently pointed out[1] that a proprietary brand of Blaud's pill, which the manufacturer claimed to be greatly superior in keeping quality to the ordinary Blaud's pill, and an ordinary commercial specimen, were each of good quality. To determine whether there is justification for the sale of ready made Blaud's pills, and to determine whether the existence of special forms of Blaud's pills is warranted, an examination of the principal market brands was undertaken. Twelve freshly purchased specimens were examined, together with a specimen of each of the three brands which were known to be several years old. Three specimens of the freshly purchased pills were what the manufacturers called "soft mass" pills.

Some of the claims made for the "soft mass' pills are:

". . . present advantage of being rapidly soluble and disintegrating in the stomach and intestinal tract. . . . Under proper storage conditions they retain their soft consistency and shape perfectly."

1. Queries and Minor Notes, THE JOURNAL A. M. A., Oct. 10, 1914, p. 1315.

"They disintegrate or dissolve readily in the digestive tract.

"They keep well, i. e., do not lose strength under proper conditions of storage.

"They show little tendency to become hard when kept under reasonable conditions.

"They are strictly true to formula."

The "soft mass" pills were "chocolate-coated." The remainder, except where stated to the contrary, were gelatin-coated. Three of the specimens (one of which was old) were not claimed to have been prepared according to the U. S. P. formula, but in general were claimed to contain the ingredients from which ferrous carbonate is produced, so that after ingestion ferrous carbonate in the "nascent" state would be formed in the alimentary tract. A number of the specimens were proprietary. These included Frosst's Blaud Capsules; Laminoids Ferruginous (nascent) Schieffelin; Laminoids Blaud (a specimen known to be at least seven years old) Schieffelin; Ferruginous Blaud, Upjohn (one of the "nascent" preparations), and two specimens of tabloids (one of which was old). The laminoids were uncoated. The tabloids were sugar-coated. With one exception all of the preparations were stated to contain 5 grains of Blaud's mass, which is equivalent to about 1 grain of ferrous carbonate. This one was a specimen of Tabloids Blaud Pill and Aloin which was known to be at least six and one-half years old. One specimen of gelatin-coated Blaud's pills (Parke, Davis & Co.) also was known to be at least six and one-half years old.

Concerning Frosst's Blaud capsules, the following claims were made:

"Blaud capsules 'Frosst' represent freshly precipitated Ferrous Carbonate of a high percentage of purity, deprived of moisture and incorporated with Castor Oil that it may be readily incapsulated in a freely soluble gelatine covering. The capsules do not harden with age nor the contents oxidize."

The cost of Frosst's Blaud capsules was nearly twice that of any other brand of Blaud's pills examined.

The following statements were made concerning Laminoids:

"The Laminoids (Ferruginous, Nascent) consist of two lamina, one of ferrous sulphate and the other of sodium bicarbonate, united by pressure. When brought in contact with water or the fluids of the stomach, chemical action at once takes place, producing fresh ferrous carbonate with the accompanying salts. An excess of carbonate is present to neutralize the acid in the stomach.

"In Laminoids (Ferruginous, Nascent) the physician will find an absolutely reliable means of administering Blaud's formula, without the possibility of the efficiency of this time-tried remedy being impaired by oxidation and the formation of more or less inert material."

The total iron content in the several preparations was determined gravimetrically, and the amount of ferrous carbonate determined by titration. In order to obtain information as to the variation among the individual pills, the assays for ferrous carbonate were made on three pills taken together and on each of three pills taken singly, or four assays in all. The average was then obtained by dividing by six. In some instances, additional assays were made. The results in some cases show considerable variation from the claimed amount of medicinal ingredients. In some of the brands the average results found by titration for ferrous carbonate were somewhat higher than those obtained by calculation from the determination of total iron. Evidently this is due to the fact that because of great variation in the weight of individual pills, uniform samples could not be obtained. The total iron content of the real Blaud pills when calculated to ferrous carbonate varied between 77 and 156 per cent. of the amount claimed, and that of the "nascent" preparation between 88 and 183.2 per cent. of the amount claimed. The determinations of ferrous carbonate did not markedly fall below this, showing that oxidation had not taken place to any considerable extent. The analytic findings are given in the accompanying table (Table 1).

In order to obtain some information as to the relative disintegrating properties of the several brands of pills, tests were carried out by treating a specimen of each (1 pill) with 90 c.c. of 0.2 per cent. hydrochloric acid at ordinary temperature in a 100 c.c. Erlenmeyer flask, and agitating the mixture by inverting once every ten minutes. This process was continued until the pill had become disintegrated, or until the experiment had continued for nine hours. In a second series of tests at the end of six hours, the acid was removed from such of the pills as had not become completely disintegrated, and 90 c.c. of a 1 per cent. solution of sodium carbonate substituted. The digestion was then continued as described above until the pill had become completely disintegrated, or until a period of six hours had elapsed. Although the disintegration would undoubtedly have taken place more rapidly at a temperature of 37 C. and possibly faster in a weak pepsin solution, it is believed that for comparative purposes the results obtained are sufficient.

The results not only showed great variation among the several brands, but also considerable variation among the several pills of the same brand. The Laminoids disintegrated the most readily, but these were not coated. The next in order were the Parke, Davis & Co. brand of soft mass pills and the Sharp & Dohme brand of soft mass pills. It should be noted that the Lilly brand of soft mass pills disintegrated more slowly than the ordinary kind from that firm. The results are given in the table (Table 1).

The results of the examination refute the commonly assumed instability of ready-made Blaud's pills. On the other hand, it is seen that the Blaud's pills of the market are not very reliable as to iron content. A range of from 77 to 182 per cent. of the claimed amount of ferrous carbonate denotes carelessness in manufacturing or lack of proper analytic control over the finished product. Further, the examination demonstrates that the "nascent" preparations, the soft mass pills, and the gelatin encapsulated oily suspension show no advantage over the ordinary kinds. In view of the findings, physicians should consider the advisability of directing the pharmacist to prepare Blaud's pills according to the U. S. P. whenever they are prescribed.

Details of Analysis

Total Iron.—This was determined by the following method: Three pills were moistened with about 3 c.c. of water, the mixture evaporated to dryness, the residue ignited until most of the carbon had been dissipated, the cooled residue digested on the water bath with hydrochloric acid containing a little nitric acid, the solution diluted, and filtered through an ash-free filter. The filter was dried, ignited, the cooled residue digested with the acid mixture as above described and the solution filtered. The united filtrates were evaporated almost to dryness, the residue diluted with water, the solution filtered, the filtrate heated, a slight excess of ammonia water added, the precipitate allowed to settle and the supernatant liquid decanted through a weighed Gooch crucible. The precipitate was then dissolved in a slight excess of diluted hydrochloric acid, a slight excess of ammonia water added to the solution, the precipitate collected in the above mentioned Gooch crucible, dried, heated and weighed as ferric oxid.

TABLE 1.—QUALITY OF COMMERCIAL BLAUD'S PILLS

Product	Manufacturer	Claims; Composition	Ferrous Carbonate Calculated from Determination of Total Iron. Per Cent. of Claim	Ferrous Carbonate (by Titration of Ferrous Iron) Per Cent. of Claim	Disintegration in Acid Solution (Hours)	Disintegration in Alkaline Solution Following Acid (Hours)
Blaud Capsules	Charles E. Frosst & Co.	5 grains, approximately ½ grain of iron in the ferrous state	77	79.2*	No effect except to dissolve coating	No effect
Blaud Pill	Sharp and Dohme	5 grains U. S. P.	91.8	92.6	6.00 5.00 6.00+	0.50
Blaud Pill Soft	Sharp and Dohme	5 grains U. S. P.	99.5	96.2	3.00 2.00 3.30 2.00	
Blaud Pill	John Wyeth and Brother	5 grains U. S. P.	114.2	113.9	8.50 6.00	
Blaud Pill	Eli Lilly & Co.	5 grains U. S. P.	117.7	112.5	3.50 2.00 4.00	
Blaud Pill Soft	Eli Lilly & Co.	5 grains U. S. P.	121.4	120.1	6.00 7.00 6.00+	1.00
Ferrous Carbonate (Blaud)	Parke, Davis & Co.	5 grains U. S. P.	117.6	121.3	4.50 4.00	
Ferrous Carbonate (Blaud) soft	Parke, Davis & Co.	5 grains U. S. P.	156.2	153.9	2.00 2.50	
Ferrous Carbonate (Blaud) (old specimen)	Parke, Davis & Co.	5 grains U. S. P.	142.3	143.7	7.00 6.00+	6.00†
Ferruginous Blaud	Wm. S. Merrell Chemical Co.	5 grains	117.4	105.9	1.00 2.00 3.00	
Ferruginous (Blaud's)	The Upjohn Company	5 grains	183.2	169.5	5.50 8.00 6.00+	4.00
Laminoids Ferruginous (nascent)	Schieffelin & Company	5 grains	121.3	126.4	1.50 2.00	
Laminoids Blaud's (old specimen)	Schieffelin & Company	5 grains	87.7	74.9	1.00 1.00	
Tabloid Blaud Pill	Burroughs, Wellcome & Co.	5 grains	104.3	104.1	7.00† 6.00+	6.00†
Tabloid Blaud Pill and Aloin (old specimen)	Burroughs, Wellcome & Co.	Blaud Pill 4 grains (20% ferrous carbonate); Aloin $\frac{1}{30}$ grain	106.1	113.1	8.50 6.00+	6.00†

* The apparent discrepancies between the amount of ferrous carbonate as calculated from the determination of total iron and that obtained by titration of ferrous carbonate are explained elsewhere in this paper.

† Not completely disintegrated in twenty-four hours.

The analytical findings in detail are given in Table 2.

Ferrous Carbonate.—This was determined according to the following method:

If three pills be dissolved in 15 c.c. of diluted sulphuric acid, a glass rod being used to break up the masses if necessary, the solution diluted with water to 100 c.c. and titrated with tenth-normal potassium dichromate, using potassium ferricyanide solution as external indicator, the amount of tenth-normal potassium dichromate consumed should indicate not less than 0.1944 gm. of ferrous carbonate, equivalent to about 1 grain of ferrous carbonate in each pill.

Some of the assays, taking three pills for the determination, were carried out in duplicate. In addition a determination was made on each of three pills taken singly in order to obtain some information as to the uniformity among the individual pills. The average value for the six pills are given in Table 1. The findings for the several assays are given in detail in Table 2.

Disintegration.—In order to obtain some information as to the relative disintegrating properties of the several brands of pills a test was carried out on each as follows:

One pill was placed in a 100 c.c. Erlenmeyer flask, 90 c.c. of 0.2 per cent. hydrochloric acid added, the flask stoppered with a cork, inverted once, the cork loosened to allow the escape of carbon dioxid, and the loosely stoppered flask allowed to remain at rest for 10 minutes. At the expiration of this time the flask was securely stoppered and agitated by inverting once. If the pill had adhered to the bottom of the flask the flask was unstoppered and the pill loosened with a glass rod after which the flask was stoppered and again inverted before allowing it another rest period. This process was repeated at intervals of 10 minutes until the pill mass was disintegrated to such an extent that the medicinal portion had been dissolved. The process was carried out in duplicate and in some instances several tests were made. As the tests were intended to be of a relative value only they were carried out at room temperature. In a second series of tests at the expiration of 6 hours the acid solution was poured from the pills that had not become completely disintegrated, 90 c.c. of 1 per cent. sodium carbonate added and the agitation continued at intervals of 10 minutes for an additional six hours as above described.

The results are given in Table 1.

Product	Manufacturer	Claims
Blaud capsules	Charles F. Frosst and Co.	5 grains, ½ grain iron in ferrous state
Blaud pill	Sharp and Dohme	5 grains U.S.P.
Blaud pill, soft	Sharp and Dohme	5 grains U.S.P.
Blaud pill	John Wyeth and Brother	5 grains U.S.P.
Blaud pill	Eli Lilly and Company	5 grains U.S.P.
Blaud pill, soft	Eli Lilly and Company	5 grains U.S.P.
Ferrous carbonate (Blaud)	Parke, Davis and Company	5 grains U.S.P.
Ferrous carbonate (Blaud) (soft)	Parke, Davis and Company	5 grains U.S.P.
Ferrous carbonate (Blaud) old specimen	Parke, Davis and Company	5 grains U.S.P.
Ferruginous (Blaud)	Wm. S. Merrell Chemical Co.	5 grains
Ferruginous (Blaud's)	The Upjohn Company	5 grains
Laminoids ferruginous (nascent)	Schieffelin and Company	5 grains
Laminoids Blaud's (old specimen)	Schieffelin and Company	5 grains
Tabloid Blaud pill	Burroughs Wellcome and Company	5 grains
Tabloid Blaud pill and aloin (old specimen)	Burroughs Wellcome and Company	Blaud pill (20% ferrous carbonate) aloin 1/20 gr.

* Average of ten pills. † A very large capsule.

Total Iron as Ferrous Carbonate (Average of 3 Pills)	Per Cent. of Claim	Ferrous Carbonate by Titration		Per Cent. of Claim	
		Average of 3 Pills	Three pills Singly	Average of 3 Pills	Three Pills Singly
0.0517 gm.	79.8	0.0518 gm.	0.0495 gm.	79.9	76.4
0.0481 gm.	74.2	0.0487 gm.	0.0529 gm.	75.2	81.6
0.0499 gm.*	77.0		0.0581 gm.†		89.6†
0.0615 gm.	94.9	0.0614 gm.	0.0616 gm.	94.7	95.0
0.0576 gm.	88.8		0.0570 gm.		87.9
			0.0575 gm.		88.7
0.0660 gm.	101.9	0.0625 gm.	0.0621 gm.	96.5	95.9
0.0630 gm.	97.2		0.0610 gm.		94.1
			0.0633 gm.		97.7
0.0742 gm.	114.5	0.0740 gm.	0.0771 gm.	114.2	119.0
0.0738 gm.	113.9		0.0748 gm.		115.5
			0.0690 gm.		106.5
0.0784 gm.	121.0	0.0706 gm.	0.0782 gm.	109.0	120.7
0.0742 gm.	114.5		0.0759 gm.		117.1
			0.0713 gm.		110.0
0.0778 gm.	120.0	0.0775 gm.	0.0782 gm.	119.6	120.7
0.0796 gm.	122.8		0.0782 gm.		120.7
			0.0782 gm.		120.7
0.0775 gm.	119.6	0.0790 gm.	0.0748 gm.	121.9	115.4
0.0749 gm.	115.6		0.0805 gm.		124.2
			0.0794 gm.		122.5
0.1005 gm.	155.1	0.0997 gm.	0.0989 gm.	153.9	152.6
0.1020 gm.	157.4		0.1001 gm.		154.4
			0.1001 gm.		154.4
0.0907 gm.	140.0	0.0958 gm.	0.0863 gm.	147.8	133.2
0.0937 gm.	144.6		0.0932 gm.		143.8
			0.0920 gm.		142.0
0.0752 gm.	116.1	0.0694 gm.	0.0667 gm.	107.1	103.0
0.0769 gm.	118.7		0.0679 gm.		104.8
			0.0690 gm.		106.5
0.1195 gm.	184.4	0.1143 gm.	0.1055 gm.	176.4	162.9
0.1180 gm.	182.1		0.1035 gm.		160.0
			0.1070 gm.		165.1
0.0912 gm.	140.7	0.0807 gm.	0.0823 gm.	124.5	126.9
0.0693 gm.	106.9	0.0863 gm.	0.0782 gm.	133.2	120.7
0.0844 gm.	130.3		0.0794 gm.		122.5
0.0696 gm.	107.4		0.0782 gm.		120.7
0.0568 gm.	87.7	0.0464 gm.	0.0506 gm.	71.6	78.1
0.0569 gm.	87.8		0.0518 gm.		79.9
			0.0495 gm.		76.4
0.0654 gm.	100.9	0.0663 gm.	0.0690 gm.	102.3	106.5
0.0698 gm.	107.7	0.0671 gm.	0.0679 gm.	103.5	104.8
			0.0701 gm.		108.2
0.0545 gm.	105.1	0.0579 gm.	0.0598 gm.	111.7	115.3
0.0555 gm.	107.1		0.0598 gm.		115.3
			0.0587 gm.		113.2

A NEW COLOR REACTION FOR PAPAVERIN

L. E. Warren, Ph.C., B.S.

(Reprinted from the Journal of the American Chemical Society, October, 1915, p. 2402)

In a study of the purity of commercial specimens of several of the opium alkaloids or their salts, a color reaction for papaverin ferricyanid was observed which, it is believed, has not hitherto been described. By modifications the test may be made to apply to the alkaloid, papaverin, or its commonly occurring salts, such as the chlorid or sulphate, so that it seems probable that the reaction may prove of value in the identification of papaverin.

Papaverin is one of the minor alkaloids of opium. It occurs in Smyrna opium to the extent of about 0.8 per cent., and in opium from other sources in amounts ranging from 0.2 to 1 per cent. Papaverin is a weak base and is much less toxic than either codein, morphin or thebain. Formerly it was not used in medicine, but, owing to the recent pharmacological and clinical researches of Pal,[1] Popper,[2] Macht[3] and others, it has attracted some attention from clinicians.

Papaverin is distinguished from the other of the more important opium alkaloids by the very sparing solubility of its ferricyanid in water and by the deep rose color which is slowly developed if the alkaloid be dissolved in sulphuric acid which contains a little formaldehyd[4] (Marquis' reagent). A number of color reactions for papaverin are described in the older literature, but it has been shown by Pictet and Kramers[5] that most of these are not due to papaverin but to cryptopin which, until recently, was present as an

1. Wien. med. Wchnschr., 1913, lxiii, 1049; Med. Times, 1914, xlii, 218.
2. Wien. klin. Wchnschr., 1914, xxvii, 361.
3. Jour. Am. Med. Assn., 1915, lxiv, 1489.
4. This reagent may be prepared by mixing 10 drops of 37 per cent. formaldehyd solution with 10 c.c. of sulphuric acid. It should not be used if more than a week or two old.
5. Ber., 1910, xliii, 1329.

impurity in most commercial papaverin. At present, however, commercial supplies of papaverin and its salts contain only traces of cryptopin.

Papaverin ferricyanid was first described by Plugge.[6] It is a pale lemon yellow compound which may be obtained as an amorphous precipitate by the addition with agitation of freshly prepared potassium ferricyanid solution to a faintly acidified, moderately dilute solution of a papaverin salt. Occasionally the precipitate separates in resin-like masses. From concentrated solutions narcotin and thebain, if present, are also precipitated as pale yellow precipitates, the narcotin salt becoming green on exposure to the air. In dilutions above 1 : 500, papaverin alone is precipitated. This method was used by Plugge for the separation of papaverin from narcotin, the two alkaloids having been previously separated from thebain by precipitation by a concentrated solution of sodium acetate.

The writer has observed that if the precipitate of papaverin ferricyanid, obtained as above described, be collected on a filter, washed with a little water and a small particle of the mass dissolved with stirring in a few drops of sulphuric acid which contains a little formaldehyd solution, a light blue color is produced at once; after a few minutes the color changes to bluish violet (sometimes purplish violet); if the solution be not further disturbed it becomes green at the edges and eventually becomes emerald green; on further standing the color fades to a dirty, brownish yellow or the solution may become nearly colorless. The reaction requires about thirty to forty minutes for completion. Good results are obtained if about 0.001 gm. of the dried papaverin ferricyanid be dissolved in about 0.1 c.c. of Marquis' reagent. The reaction does not occur if sulphuric acid which does not contain formaldehyd be used, although a purplish color may be produced. Hexamethylenamin may be used in place of formaldehyd solution, although the initial color is somewhat slow in appearing and may be greenish blue

6. Arch. Pharm., 1887, ccxxv, 344 and 809.

rather than blue. Other reducing agents, such as formic acid, phenylhydrazin hydrochlorid, sodium sulphite or sodium thiosulphate, if used in place of formaldehyd, do not give the reaction.

The test was applied to the ferricyanids of several of the alkaloids which form sparingly soluble ferricyanids. The cephaelin and emetin salts gave no colors; the narcotin salt gave a fugitive violet; the strychnin salt gave the well-known "fading purple" reaction. In the last two experiments the presence of formaldehyd did not appear to have any influence in the reaction, as the colors were given by the alkaloidal salts and sulphuric acid without that reagent.

The test was then varied by mixing finely powdered papaverin alkaloid with finely powdered potassium ferricyanid and stirring the mixture with Marquis' reagent. With some variations the succession of colors above noted, blue (greenish blue; see below), violet, green and brownish yellow, was produced, and the deep rose color, characteristic of papaverin with Marquis' reagent, did not appear. In this case it was noted that the initial color was a faintly greenish blue rather than a pure blue and in some instances the emerald green stage was not very pronounced, the violet being succeeded by the brownish yellow color. Potassium ferrocyanid can not be substituted for the ferricyanid in the reaction.

The test (alkaloid + potassium ferricyanid + Marquis' reagent) was then applied to a considerable number of alkaloids or their salts. In most cases either no color was produced or the color was not different from the control in which no potassium ferricyanid was used. The substances studied were:

Aconitin, apomorphin hydrochlorid, atropin sulphate, berberin hydrochlorid, beta-eucain lactate, brucin, caffein, cephaelin hydrochlorid, cinchonidin, cinchonin, cocain hydrochlorid, codein, colchicin, coniin hydrobromid, dionin, emetin hydrochlorid, mixed alkaloids from gelsemium, heroin, homatropin hydrobromid, hydrastin, morphin, narcein, nicotin, novocain, physostigmin sulphate, pilocarpin hydrochlorid,

pseudomorphin, pyridin, quinin, sanguinarin nitrate, solanin, spartein sulphate, strychnin, thebain, theobromin, and the mixed alkaloids from veratrum.

None of the alkaloids tried except berberin, brucin, colchicin, hydrastin and physostigmin gave reactions differing markedly from the controls. Berberin gave a chocolate brown color, the control being lemon yellow; brucin, an orange-red color with colorless control; colchicin a reddish brown color with yellow control; hydrastin a brownish red color with colorless control; and physostigmin a pale, brownish yellow color with colorless control. No attempt was made to determine whether the color reactions noted with the last-named alkaloids had been previously described or whether they were characteristic. In no case was there a duplication or simulation of the reaction with papaverin noted earlier in this paper.

The experiment with papaverin was then varied by substituting various oxidizing agents, such as ammonium vanadate, manganese dioxid, potassium permanganate, selenious acid, etc., for the potassium ferricyanid, in each case a very small quantity of the finely powdered reagent being well mixed with the finely powdered alkaloid and the mixture thoroughly stirred into a few drops of Marquis' reagent. Color reactions were given with a considerable number of the reagents tried, the colors in general being about the same as with potassium ferricyanid, with some individual variations in shade. Reactions were given by ammonium vanadate, cerium oxid, ferric ammonium sulphate, ferric chlorid (solid), lead peroxid, manganese dioxid, phosphomolybdic acid, potassium bromate, potassium chlorate, potassium dichromate, potassium iodate, potassium nitrate, selenious acid, silver nitrate, sodium ortho-arsenate and uranium nitrate. Of these, the colors produced by the iron, silver and uranium salts were not very satisfactory. Bromates, chlorates, and nitrates were, in general, found not to give good results, as the oxidation apparently was carried out too rapidly to give a satisfactory play of colors.

Ammonium molybdate, ammonium persulphate, magnesium peroxid, phosphotungstic acid or mercuric oxid did not give the reaction. Of the oxidizing reagents tried ammonium vanadate, cerium oxid, potassium permanganate and selenious acid were, perhaps, as satisfactory as any.

One of the most striking reactions observed was obtained by using potassium permanganate as the oxidizer. A very small crystal of the salt was crushed with a glass rod, about 0.0005 gm. of papaverin intimately mixed with the powder and the mixture stirred into about 0.2 c.c. of Marquis' reagent. A green color appeared which almost instantly became blue. This deepened into an intense violet-blue which after some time became bluish green, then green and later a dirty brown.

Each of the alkaloids to which the test had been applied, using potassium ferricyanid as the oxidizing agent, was then tested by separately employing ammonium vanadate and potassium permanganate. In no case was there a duplication of the papaverin reaction, although codein and dionin gave colors which were somewhat confusing. By making comparisons with papaverin, however, distinct differences were observable.

After the work recorded above had been completed the author received from Prof. John Uri Lloyd a specimen of an unnamed alkaloid (possibly a mixture of alkaloids) which Professor Lloyd had separated from sanguinaria. The author also prepared the alkaloidal material according to the directions of Professor Lloyd from sanguinaria extracts sent by him for the purpose. On applying the papaverin test to this alkaloidal separate it was found that with certain oxidizing agents the succession of colors produced was somewhat like that with papaverin. Consequently some confusion might result unless comparison tests be carried out with known papaverin. With sodium ortho-arsenate, manganese dioxid, potassium dichromate and potassium iodate the unnamed alkaloidal sub-

stance gave an intense emerald green color which soon showed bluish streaks and faded through green to a dirty, yellowish brown. With the same reagents papaverin gave a momentary greenish blue which passed through deep blue, violet-blue, to green and brownish yellow. However, if selenious acid be used as the oxidizing reagent the initial color produced by the unnamed alkaloidal separate is an intense purplish violet, instead of a fugitive greenish blue which becomes deep blue, as with papaverin. The unnamed alkaloid is further differentiated from papaverin by its solubility in ammonia water, the comparatively ready solubility of its ferricyanid in water, and by the purplish violet, instead of a deep rose color, which it gives with Marquis' reagent.[7]

Although the number of alkaloids to which the newly described test was applied is too small to warrant the conclusion that the reaction described is characteristic for papaverin, yet the considerable number tested without duplication of the color succession leads the author to believe that the reaction may prove of value in the identification of papaverin.

SUMMARY

1. Very few characteristic color reactions for papaverin are known, the most satisfactory being the deep rose produced by Marquis' reagent.

2. By treating papaverin ferricyanid with Marquis' reagent a blue color is produced which passes through violet and green stages to a dirty, brownish yellow.

3. By treating a mixture of the alkaloid, papaverin, and potassium ferricyanid with Marquis' reagent an essentially identical reaction is produced, although the initial color is generally greenish blue.

4. Many other oxidizing agents may be used in place of potassium ferricyanid, the shades of color produced varying somewhat with the reagent employed.

7. At the request of Professor Lloyd the properties of this unnamed alkaloidal separate from sanguinaria are being further investigated and the results will be reported in a separate paper.

5. The reaction is best observed by intimately mixing a very small quantity of papaverin with a very small quantity of an oxidizing agent, such as cerium oxid, phosphomolybdic acid or potassium permanganate, and stirring the mixture with a few drops of sulphuric acid containing a little formaldehyd.

6. Of thirty-nine alkaloids tested, but one (unnamed alkaloidal separate from sanguinaria) gave colors which in any way simulated the reaction with papaverin.

7. By using selenious acid as the oxidizing agent the unnamed sanguinaria alkaloid (or alkaloids) may be differentiated readily from papaverin.

The thanks of the author are due to Prof. John Uri Lloyd for specimens of alkaloids from gelsemium, tobacco, sanguinaria and veratrum kindly furnished by Professor Lloyd for the investigation. Also to Dr. Willis S. Hilpert for verifying some of the reactions.

AN EXAMINATION OF SEVERAL COMMERCIAL SPECIMENS OF OPIUM ALKALOIDS OR THEIR SALTS

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For several years the question of the synergistic effects of drugs has attracted considerable attention, particularly in connection with the several alkaloids of opium. Although about twenty-five alkaloids have been isolated from opium, the quantities in which most of the "minor alkaloids" exist in that drug are so minute that most of the pharmacologic experiments in synergism have been carried out with the alkaloids which occur in the largest amounts;[1] that is, with

1. According to Henry ("The Plant Alkaloids," 1913, p. 199), the opium which is used in America and Europe is almost wholly of the Asia Minor variety (Smyrna opium). The names and formulæ of the opium bases and the approximate amounts in which they occur in Smyrna opium are given in Appendix 1.

morphin, narcotin, papaverin, thebain, codein, and narcein.

Dr. D. I. Macht, of the Department of Pharmacology of Johns Hopkins University, has conducted pharmacologic studies[2] on some of the opium alkaloids. This work was carried out under a grant from the Committee on Therapeutic Research of the Council on Pharmacy and Chemistry of the American Medical Association. In view of the fact that the Laboratory of the American Medical Association has often shown that little-used drugs are likely to be of poor quality,[3] it was thought best to examine the material used by Dr. Macht for identity and purity.

The specimens examined were codein phosphate, morphin sulphate, narcein, narcotin, narcotin hydrochlorid, papaverin hydrochlorid, and thebain hydrochlorid. Dr. Macht stated that all of the material was of the Merck brand except one specimen of morphin sulphate, one specimen of narcotin, and a specimen of papaverin hydrochlorid.[4] These were products bearing the labels, respectively, of Eimer & Amend, the Mallinckrodt Chemical Works, and the Hoffmann-LaRoche Chemical Works.

With the exception of codein phosphate and morphin sulphate, which are described in the U. S. Pharmacopeia,[5] the tests for the purity of the opium bases or their salts are not described in the literature with sufficient exactness to be of much use in determining the purity of commercial products. Therefore it became necessary to compile or devise tests by which the identity and purity of the specimens sent

2. Jour. Am. Med. Assn., 1915, lxiv, 477 and 1489.

3. Unofficial Preparations of Hydrastis (Golden Seal), Rep. Chem. Lab., A. M. A., 1908, i, 23. Examination of Tablets of Bismuth, Opium and Phenol., Rep. Chem. Lab., A. M. A., 1908, i, 28. Zinc Permanganate, Rep. Chem. Lab., A. M. A., 1909, ii, 15. The Composition of Commercial Copper Citrate, Rep. Chem. Lab., A. M. A., 1910, iii, 27. The composition of Strychnin Arsenate, Rep. Chem. Lab., A. M. A., 1910, iii, 35. Aromatic Digestive Tablets, Rep. Chem. Lab., A. M. A., 1910, iii, 64.

4. An additional specimen of papaverin hydrochlorid bearing the Merck label was examined later and the results are included in this report. This brand of papaverin hydrochlorid was not used by Dr. Macht.

5. Pharmacopeia of the United States, 8th rev., pp. 109 and 295.

could be judged. Accordingly preliminary tests were prepared which were based upon published information. These were amplified and modified as found necessary by the results obtained in the examination as the work progressed. As the quantities of material sent by Dr. Macht were small, most of the preliminary tests were carried out on specimens purchased from the same wholesale druggist from whom Dr. Macht had obtained his supplies. In so far as it was possible to obtain them, the purchased specimens were of the same brands as were used by Dr. Macht. One specimen of narcotin which was stated by Dr. Macht not to be a market preparation, but to have been prepared by the manufacturer for research purposes, was not duplicated. Also a second specimen of thebain hydrochlorid could not be obtained.

The tests to which the specimens of narcein, narcotin, narcotin hydrochlorid, papaverin hydrochlorid and thebain hydrochlorid were subjected were adapted and devised, for the most part, from published information concerning the properties of the respective substances; the properties of such other substances as seemed likely to be present as impurities were also taken into account.

CODEIN PHOSPHATE

The tests to which the specimens of codein phosphate were subjected were essentially those which will probably be described in the ninth revision of the U. S. Pharmacopeia.[6] In addition, phosphate was determined in the solution from which the codein had been removed, by precipitation as ammonium magnesium phosphate, heating and weighing as magnesium pyrophosphate.

The results obtained in the examination are given below.

The specimen of codein phosphate was a fine, white powder which under the microscope was seen to be

6. Jour. Am. Pharm. Assoc., 1913, ii, 1389.

considerably effloresced. It dissolved in water, leaving not more than traces of insoluble matter. The specimen was free from chlorids, sulphates, meconates, cryptopin, thebain, and morphin. A purchased specimen of codein phosphate appeared to be of as good quality as the one sent by Dr. Macht. It was not effloresced to such a great extent. The findings for the two specimens are given in Table 1.

Codein phosphate was first studied by Anderson,[7] who obtained it containing one and one-half molecules of water of hydration. It was pointed out by Schmidt,[8] a number of years ago, that commercial codein phosphate was of variable composition.

TABLE 1.—COMPOSITION OF TWO SPECIMENS OF COMMERCIAL CODEIN PHOSPHATE

	Merck	Merck*	Theory
Water (loss at 100 C.)	2.68	8.61[a]	8.31[b]
Alkaloid	74.13	70.15	69.06
Phosphoric acid (H_3PO_4)	23.75	22.90	22.63
Melting-point of isolated alkaloid	155.3 C. (corr.)	155.7 C. (corr.)	154 to 156 C.

* Purchased specimen.

[a], [b]. Codein phosphate crystallized with two molecules of water of hydration contains 8.31 per cent. of water of hydration; with one and one half molecule, 6.36 per cent.

Depending upon the method of preparation, it might contain one-half, one and one-half, or two molecules of water of hydration. Schmidt states that codein phosphate effloresces rapidly at ordinary temperature, losing all but one-half molecule of its water of hydration. He contends that in the interest of stability and uniform dosage the salt having the latter composition should be officialized.

The U. S. Pharmacopeia (VIII) describes codein phosphate as containing two molecules of water of hydration, but states that the salt frequently crystallizes with one and one-half molecules of water of hydration.

7. Ann. Chem. Pharm., 1851, lxxxii, 252.
8. Apoth. Ztg., 1890, v, 366.

MORPHIN SULPHATE

The tests to which the specimens of morphin sulphate were subjected were essentially those which will probably be described in the ninth revision of the U. S. Pharmacopeia.[9] In addition, sulphate was determined by precipitation with barium chlorid, collection of the barium sulphate, heating and weighing in the usual way. Codein sulphate was calculated from the amount of codein as determined.

The results obtained in the examination are given below.

Two specimens of morphin sulphate were received from Dr. Macht and examined. Each was a yellowish-white, crystalline powder which dissolved in water to a pale yellow, neutral solution, leaving not more than traces of insoluble matter. Each specimen was free from ammonium salts, chlorids, cryptopin, meconates, narcotin, and thebain. Each specimen contained small quantities of a codein salt.

The specimens were compared with a purchased specimen of morphin sulphate. Each was considerably darker in color than the one purchased, and the solution of each in water was considerably darker. The specimens sent contained less codein than the specimen purchased. The analytical results were also compared with those obtained from a specimen of morphin sulphate of another brand (Powers-Weightman-Rosengarten) which was known to be several years old. The analytical findings are given in Table 2.

The results of the examination show that the chief impurity in the specimens of morphin sulphate examined is codein sulphate. The presence of codein in the market supply of morphin sulphate has repeatedly been shown.[10] Up to 7 per cent. has been reported, but the amounts usually found are less than

9. Jour. Am. Pharm. Assoc., 1913, ii, 1397.

10. Williams: Am. Jour. Pharm., 1912, lxxxiv, 391. Kebler, ibid., 501. Williams: Jour. Am. Pharm. Assoc., 1913, ii, 81. Kebler, Jour. Am. Pharm. Assoc., 1912, i, 1405. Kebler: Proc. Assoc. Off. Agric. Chem., 1913, xxix, 192. Wilson: Ann. Rep. U. S. Agric. (1912). E'We and Vanderkleed: Jour. Am. Pharm. Assoc., 1913, ii, 981.

3 per cent. The ninth revision of the U. S. Pharmacopeia[11] will probably provide a test for the presence of codein sulphate in morphin sulphate which will limit the permitted amount to not more than about 1 per cent. of the foreign salt. The specimens sent by Dr. Macht conform to this standard.

In addition to the tests proposed for inclusion in the ninth revision of the U. S. Pharmacopeia, very few experiments were carried out with morphin sulphate. The optical activity of one of the specimens was observed and was found not to agree with the pub-

TABLE I.—COMPOSITION OF SOME SPECIMENS OF COMMERCIAL MORPHIN SULPHATE

	Merck	Eimer & Amend	Merck*	P.-W.-R.†	Theory
Water (loss at 105° C. in vacuum)	11.22	11.59	11.11	11.03	11.88
Sulphuric acid (H_2SO_4)	13.15	12.99	13.03	12.99	12.93
Codein (anhydrous alkaloid)	0.41[a]	0.58[b]	1.26[c]	2.41[d]	0
Morphin (anhydrous alkaloid by difference)	75.22	74.84	74.60	73.57	75.19

* Purchased specimen.
† Purchased specimen; known to be several years old.
[a] Equivalent to 0.54 per cent. of crystallized codein sulphate.
[b] Equivalent to 0.76 per cent. of crystallized codein sulphate.
[c] Equivalent to 1.65 per cent. of crystallized codein sulphate.
[d] Equivalent to 3.17 per cent. of crystallized codein sulphate.

lished values. For example, Henry[12] gives the specific rotatory power of the salt as — 100.47° in water at 15 C. The value found for the purchased specimen of the salt (Merck brand) was — 93.44°, or about 93 per cent. of theory. The specific rotatory power of another purchased specimen of the salt (P.-W.-R. brand known to be several years old) was found to be — 94.07°. The former of these contained about 1.65 per cent. of codein sulphate and the latter about 3.17 per cent., but as the specific rotatory power of crystallized codein sulphate is stated[13] to be

11. Jour. Am. Pharm. Assoc., 1913, 6, 1397.
12. "The Plant Alkaloids," p. 211.
13. Ibid., p. 214.

101.2° at 15 C. the discrepancy noted in the morphin salt can scarcely be explained on the ground of the presence of this impurity.

NARCEIN

In addition to tests for identity, the tests applied to the specimens of narcein included determinations of water of hydration (loss at 100 C.), chlorid, and melting-point. Limit tests were carried out for meconates, sulphates, codein, morphin, narcotin, and papaverin. Codein, narcotin, and papaverin were tested for by dissolving the alkaloid in potassium hydroxid solution, extracting the solution with ether, and testing the residue on evaporation for the respective alkaloids.

The results obtained in the examination of the specimen of narcein are given below.

Grayish-white powder which under the microscope was seen to be considerably effloresced. The preparation was free from sulphates, meconates, narcotin, codein, and morphin, but contained considerable quantities of a chlorid, evidently narcein hydrochlorid. The findings were compared with those obtained from the examination of a purchased specimen. The two specimens were not markedly different. The analytical findings for the specimens are given in Table 3.

Because of the similarity between the solubilities of narcein and narcein hydrochlorid it is very difficult to separate the two substances by means of solvents. Consequently commercial narcein is usually contaminated with this impurity. E. Merck[14] is of the opinion that a preparation which is free from meconin and which does not melt below 165 C. is of sufficient purity for most purposes.

Narcein is distinguished from codein by its weak basic properties, its scant solubility in most of the ordinary organic solvents, by the formation of a blue instead of a reddish-brown precipitate with very dilute iodin solution; by the production of a brown instead of a violet color with Mar-

14. Chem. Ztg., 1889, xiii, 525.

quis' reagent, and a light brown instead of a green color with Lafon's reagent; from morphin by its weak basic properties, its failure to reduce iodic acid, its comparatively ready solubility in hot water and in ammonia water, by the formation of a blue instead of a reddish-brown precipitate with very dilute iodin solution, by the production of a brown instead of a purple color with Marquis' reagent, a brownish-green instead of a purple color with Fröhde's reagent, and a light brown instead of a blue color with Lafon's reagent; from narcotin by its scant solubility in most of the ordinary organic solvents, its comparatively easy solubility in hot water or in ammonia water, by the formation of a blue instead of a reddish-brown precipitate with very dilute iodin solution, by the production of a brown instead of a green color with Lafon's reagent, and a brown instead of an orange color with Mandelin's reagent; from papaverin

TABLE 3.—COMPOSITION OF TWO SPECIMENS OF COMMERCIAL NARCEIN

	Merck	Merck[a]	Theory $C_{23}H_{27}O_9N.3H_2O$
Water (loss at 100 C.)	6.32	6.13	10.81
Hydrochloric acid (HCl)	1.20[a]	0.06[b]	0
Alkaloid (by difference)	92.48	92.89	89.19
Melting-point (undried specimen)	165 C. (corr.)	165 C. (corr.)	170 C.

[a] Purchased specimen.
[a] Equivalent to 17.73 per cent. of narcein hydrochlorid ($C_{23}H_{27}O_9N.HCl.3H_2O$).
[b] Equivalent to 14.43 per cent. of narcein hydrochlorid.

by its scant solubility in most of the organic solvents, its comparatively easy solubility in hot water or in ammonia water, by the formation of a blue instead of a reddish-brown precipitate with very dilute iodin solution, by the production of a brown instead of a deep rose color with Marquis' reagent, a brown instead of a greenish-blue color with potassium ferricyanid and Marquis' reagent, and a light brown instead of a green color with Lafon's reagent; from thebain by its weak basic properties, its comparatively easy solubility in hot water or in ammonia water, its scant solubility in most of the ordinary organic solvents, by the formation of a blue instead of a reddish-brown precipitate with very dilute iodin solution, the formation of an orange-red instead of a reddish-brown coloration with chlorin water and ammonia water, and by the production of a yellow instead of a deep blood-red color with sulphuric acid.

NARCOTIN

The tests to which the specimens of narcotin were subjected included limit tests for chlorid, meconates, sulphates, codein, morphin, papaverin, and thebain, as well as a determination of the melting-point of the dried alkaloid.

The results obtained are given herewith.

Two specimens of narcotin were received. One (Merck) was a white crystalline powder, the other (M. C. W.) in the form of colorless prisms. The latter was stated not to be a market preparation, but to have been prepared by the manufacturer for research purposes. Portions of each specimen dissolved in diluted hydrochloric acid without residue. Each was free from chlorid, sulphates, meconates, codein, morphin, papaverin, and thebain.

Narcotin is distinguished from codein by its weak basic properties, its scant solubility in water or in ammonia water, by the production of a pale, evanescent violet instead of a deep, bluish-violet color with Marquis' reagent, and an orange-red instead of a pale green color with Mandelin's reagent; from morphin by its weak basic properties, its ready solubility in ether, chloroform, and benzene, its failure to reduce iodic acid, by the production of a yellowish-green instead of a purple color with Fröhde's reagent, and a pale, evanescent violet instead of a deep purple color with Marquis' reagent; from narcein by the formation of a brownish-red instead of a blue precipitate with very dilute iodin solution; from papaverin by the production of a pale, evanescent violet instead of a deep rose color with Marquis' reagent, and a dirty, evanescent violet instead of a greenish-blue color with potassium ferricyanid and Marquis' reagent; and from thebain by its weak basic properties and by the production of a pale, evanescent violet instead of a deep blood-red color with Marquis' reagent.

The Merck specimen melted at 175.3 C. (corr.).

The M. C. W. specimen melted at 174 C. (corr.).

A purchased specimen of narcotin (Merck) melted at 174.6 C. (corr.).

Comparison of the other findings with those obtained from the purchased specimen of narcotin showed no material differences.

The results, therefore, indicate that the specimens are of good quality.

NARCOTIN HYDROCHLORID

The tests to which the specimen of narcotin hydrochlorid was subjected were essentially the same as for narcotin. Narcotin alkaloid was determined by dissolving the salt in water, making the solution alkaline, shaking with chloroform, evaporating the chloroform extracts, drying the residue, and weighing. In addition to the other tests, chlorid was determined in the solution from which the alkaloid had been removed by acidifying with nitric acid, precipitating with silver nitrate, drying the precipitate, and weighing the silver chlorid.

The results obtained in the examination are given below.

White powder; soluble in water without residue. The specimen was free from sulphates, meconates, codein, morphin, and papaverin.

Comparison of the findings with those obtained from a purchased specimen of narcotin hydrochlorid showed that there were no appreciable differences.

The findings for the two specimens are given in Table 4.

The ready solubility of codein in water and in ammonia water suggested that this property might be utilized for the detection of small quantities of codein in presence of relatively large quantities of those alkaloids which are very insoluble in water, such as narcotin and papaverin.[15] Accordingly several mixtures in known proportions of codeine and the named alkaloids or their salts were prepared. In each case the mixture was dissolved in 50 Cc. of water, containing a few drops of hydrochloric acid, a very slight excess

15. This method has long been used for approximately separating morphin from codein.

of diluted ammonia water added with stirring, the mixture set aside for about eighteen hours, the precipitate collected in a weighed Gooch crucible, dried and weighed. The filtrate was then shaken with successive portions of ether until extraction was complete, the ether extracts united, washed with water, evaporated, the residue dried and weighed. Controls were carried out with the respective alkaloids or their salts without admixture with codein. The alkaloidal residues from the controls amounted to but a few milligrams in each case. If this quantity were subtracted from the residue obtained from the extraction of the codein mixture it was found that the remainder was a close approximation to the quantity of codein taken.

TABLE 4.—COMPOSITION OF TWO SPECIMENS OF COMMERCIAL NARCOTIN HYDROCHLORID

	Merck	Merck*	Theory $C_{22}H_{23}O_7N.HCl$
Hydrochloric acid (HCl)	8.41	7.88	8.11
Anhydrous alkaloid	89.47	91.1	91.89
Melting-point of isolated alkaloid	174 C. (corr.)	174 C. (corr.)	174 C.-176 C.

* Purchased specimen.

Results.—From 0.2596 gm. of narcotin, a precipitate weighing 0.2569 gm. was obtained, equivalent to 98.96 per cent. of the amount of narcotin taken, and an anhydrous ether extract residue weighing 0.0038 gm. was obtained equivalent to 1.46 per cent. of the quantity taken. The ether extract residue gave tests for narcotin, but did not respond to tests for codein. From 0.2515 gm. of narcotin to which 0.0267 gm. of anhydrous codein had been added, a precipitate weighing 0.2494 gm. was obtained, equivalent to 98.37 per cent. of the amount of narcotin taken, and an anhydrous ether extract residue weighing 0.0270 gm. was obtained, equivalent to 101.1 per cent. of the amount of codein taken. From 0.1644 gm. of narcotin a precipitate weighing 0.1622 gm. was obtained, equivalent to 98.66 per cent. of the amount

of narcotin taken. The filtrate gave an ether extract residue weighing 0.0017 Gm., or 1.03 per cent. of the quantity of narcotin taken. This gave tests for narcotin, but did not respond to tests for codein. From 0.2315 gm. of narcotin a precipitate weighing 0.2305 gm. was obtained, equivalent to 98.71 per cent. of the amount of narcotin taken. The ether extract weighed 0.0020 gm., equivalent to 0.86 per cent. of the quantity of narcotin taken. The residue responded to tests for narcotin, but not to tests for codein. From 0.2286 gm. of narcotin to which 0.0233 gm. of anhydrous codein had been added, a precipitate weighing 0.2272 gm. was obtained, equivalent to 99.39 per cent. of the quantity of narcotin taken; and an ether extract weighing 0.0232 gm. was obtained, equivalent to 99.57 per cent. of the quantity of codein taken.

From these tests it can be seen that the presence of small quantities of codein in narcotin can be detected readily by the method, and, further, can even be determined with a moderate degree of accuracy.

PAPAVERIN HYDROCHLORID

The tests to which the specimens of papaverin hydrochlorid were subjected included identification, determinations of the alkaloid and chlorid, melting-point of the isolated alkaloid, and qualitative tests for sulphates, meconates, codein, cryptopin, narcotin, and morphin.

In addition to the specimen of papaverin hydrochlorid sent by Dr. Macht and the one purchased, a specimen of the salt was included in the examination which had been submitted by its manufacturer to the Council on Pharmacy and Chemistry for inclusion with New and Nonofficial Remedies. The results obtained in the examination of the several specimens are given below.

Each of the specimens was a white, crystalline, odorless powder, which dissolved in water without leaving any residue to form a clear solution having an acid reaction. Each of the specimens was free from sul-

phates, meconates, codein, and morphin, but two of them appeared to contain traces of cryptopin. The findings for the three specimens are given in Table 5.

In 1910 Pictet and Kraemers[16] pointed out that most of the color reactions for papaverin described in the literature were not due to that alkaloid, but to cryptopin, which at that time was present as an impurity in commercial papaverin to the extent of as high as 4 per cent. These authors obtained pure papaverin in the form of its acid oxalate by precipitating with oxalic acid in the presence of alcohol. The cryptopin was then recovered from the filtrate by making alkaline

TABLE 5.—COMPOSITION OF THREE SPECIMENS OF PAPAVERIN HYDROCHLORID

	Roche	Roche*	Merck†	Theory $C_{20}H_{21}O_4N.HCl$
Moisture	.....	0.14	0.12	0
Alkaloid	90.18	90.41	90.38	90.30
Hydrochloric acid (HCl)	9.75	9.73	9.84	9.70
Melting-point of isolated alkaloid	146.8 C. (corr.)	146.7 C. (corr.)	147.3 C. (corr.)	147 C.

* Purchased specimen.
† Specimen submitted to the Council on Pharmacy and Chemistry.

and shaking with appropriate solvents. The papaverin was recovered from the oxalate by dissolving in hot water, making alkaline and shaking with appropriate solvents.

Papaverin is distinguished from codein by its weak basic properties, its scant solubility in water or in ammonia water, by the production of a deep rose instead of a violet color with Marquis' reagent and a greenish-blue instead of a violet color with potassium ferricyanid and Marquis' reagent; from morphin by its weak basic properties, its ready solubility in most of the ordinary organic solvents, its failure to reduce iodic acid, by the production of a deep rose instead of a purple color with Marquis' reagent; and a greenish-blue instead of a purple color with potassium ferricyanid and Marquis' reagent; from narcein by its ready solubility in most of the ordinary organic solvents,

16. Ber., 1910, xliii, 1329.

by its scant solubility in hot water or in ammonia water, by the formation of a reddish-brown instead of a blue precipitate with very dilute iodin solution, by the production of a deep rose instead of a brown color with Marquis' reagent, and a greenish-blue instead of a brown color with potassium ferricyanid and Marquis' reagent; from narcotin by the production of a deep rose instead of a fugitive violet color with Marquis' reagent, and a greenish blue instead of a dirty, evanescent violet color with potassium ferricyanid and Marquis' reagent; and from thebain by its weak basic properties, by the production of a colorless instead of a deep blood-red solution with sulphuric acid, a deep rose instead of a deep blood-red color with Marquis' reagent, and a greenish-blue instead of a deep blood-red color with potassium ferricyanid and Marquis' reagent.

In testing the specimens of papaverin hydrochlorid for traces of cryptopin salts it was found desirable to remove the papaverin as completely as possible, so as to leave the cryptopin in as high concentration as possible. Precipitation as acid oxalate was tried, but was found not to be as satisfactory as precipitation by potassium ferricyanid to form the acid papaverin ferricyanid. This was collected in a weighed Gooch crucible, washed with a little water, dried at 100 C., and weighed. The filtrate was made alkaline with ammonia water, the mixture shaken with chloroform, the solvent washed with water, evaporated, the residue dried at 100 C., and weighed. If the quantities of papaverin hydrochlorid taken for the test lay between 0.2 and 0.3 gm., the residues obtained by this method usually amounted to less than 2 per cent. The residue in all cases consisted principally of papaverin which had escaped precipitation. From the violet color produced by solution in sulphuric acid it was concluded that traces of cryptopin were present in two of the residues. Codein was not present in any. The following results were obtained:

From 0.2842 gm. of papaverin hydrochlorid, equivalent to 0.2566 gm. of papaverin, 0.3103 gm. of papaverin ferricyanid was obtained, equivalent to 0.2535 gm. of papaverin, or 98.77 per cent. of the

theoretical amount. From the filtrate a residue weighing 0.0032 gm. was obtained, equivalent to 1.25 per cent. of the alkaloid taken. From 0.3282 gm. of papaverin hydrochlorid, equivalent to 0.2964 gm. of papaverin, 0.3521 gm. of papaverin ferricyanid was obtained, equivalent to 0.2907 gm. of papaverin, or 98.07 per cent. of the theoretical amount. From the filtrate a residue weighing 0.0065 gm. was obtained, equivalent to 1.98 per cent. of the alkaloid taken.

Tests for codein were made by the water solubility method already described under narcotin hydrochlorid. The following results were obtained:

From 0.5028 gm. of papaverin hydrochlorid, equivalent to 0.4540 gm. of papaverin, a precipitate weighing 0.4560 gm. was obtained, equivalent to 100.44 per cent. of the theoretical amount of papaverin taken. The filtrate gave an anhydrous ether extract residue weighing 0.0032 gm., or 0.71 per cent. of the theoretical quantity of papaverin taken. This residue gave tests for papaverin, but no satisfactory tests for codein or cryptopin could be obtained. From 0.2070 gm. of papaverin hydrochlorid, equivalent to 0.1869 gm. of papaverin, a precipitate weighing 0.1857 gm. was obtained, equivalent to 99.04 per cent. of the theoretical amount of papaverin taken. From the filtrate an anhydrous ether-extract residue was obtained weighing 0.0014 gm., equivalent to 0.75 per cent. of the theoretical amount of papaverin taken. From 0.2255 gm. of papaverin hydrochlorid, equivalent to 0.2036 gm. of papaverin, to which 0.0121 gm. of anhydrous codein had been added, a precipitate weighing 0.2010 gm. was obtained, equivalent to 98.72 per cent. of the theoretical amount of papaverin taken. From the filtrate an anhydrous ether-extract residue weighing 0.0142 gm. was obtained, equivalent to 117.3 per cent. of the amount of codein taken. This residue gave tests for papaverin and for codein.

It is evident, therefore, that the method can be used for the detection of small quantities of codein in much

larger quantities of papaverin, and can even be employed to approximately separate the two alkaloids from each other in such mixture.

THEBAIN HYDROCHLORID

The tests to which the specimens of thebain hydrochlorid were subjected included determinations of the water of hydration (loss at 100 C. in a partial vacuum), of the alkaloid, and of the chlorid; the application of limit tests for meconates, sulphates, papaverin, and morphin.

The results obtained in the examination are given below.

TABLE 6.—COMPOSITION OF A SPECIMEN OF COMMERCIAL THEBAIN HYDROCHLORID

	Merck	Theory $C_{19}H_{21}O_3N.HCl$
Water (loss at 100 C. in vacuum)	4.22	4.93
Anhydrous alkaloid	85.20	85.10
Hydrochloric acid (HCl)	9.98	9.97
Melting-point of isolated alkaloid	193.2 C. (corr.)	193 C.

But one specimen of thebain hydrochlorid was examined: faintly yellowish, odorless, rhombic prisms, which yielded a white powder on crushing. The salt dissolved in water, forming a colorless, neutral solution. Meconate, sulphates, papaverin, and morphin were absent. The analytical findings are given in Table 6.

Because of the more ready solubility of thebain in water, as compared with narcotin and papaverin, it was found that the water-solubility test could not be used to separate thebain from codein. The method was tried as described for narcotin, but the results were not encouraging, as is shown by the findings given below.

From 0.2329 gm. of thebain hydrochlorid, equivalent to 0.1982 gm. of anhydrous alkaloid, a precipitate weighing 0.1497 gm. was obtained, equivalent to 75.43

per cent. of the quantity of thebain taken. From the filtrate an anhydrous ether-extract residue weighing 0.0482 Gm. was obtained, equivalent to 24.32 per cent. of the amount of thebain taken. From 0.2033 gm. of thebain hydrochlorid, equivalent to 0.1730 gm. of anhydrous thebain, to which 0.0229 gm. of anhydrous codein had been added, a precipitate weighing 0.1225 gm. was obtained, equivalent to 70.80 per cent. of the amount of thebain taken. From the filtrate an anhydrous ether-extract residue weighing 0.7313 gm. was obtained, equivalent to 311.3 per cent. of the quantity of codein taken.

Thebain is distinguished from codein by its scant solubility in water or in ammonia water, and by the production of a deep blood-red instead of a violet color with Marquis' reagent; from morphin by its ready solubility in most of the ordinary organic solvents, its failure to reduce iodic acid, by the production of a yellow instead of an orange-red color with nitric acid, and a deep blood-red instead of a purple color with Marquis' reagent; from narcein by its scant solubility in water or in ammonia water, its ready solubility in most of the ordinary organic solvents, by the production of a brownish-red instead of a blue precipitate with very dilute iodin solution, a reddish-brown instead of an orange-red color with chlorin water and ammonia water, and a brown instead of a deep blood-red color with Marquis' reagent; from narcotin by its strong basic properties, and by the production of a deep blood-red instead of a fugitive violet color with Marquis' reagent; and from papaverin by its strong basic properties, by the production of a deep blood-red instead of a deep rose color with Marquis' reagent, and a deep blood-red instead of a greenish-blue color with potassium ferricyanid and Marquis' reagent.

The analytical findings indicate that the quality of some of the specimens examined is fair and of some excellent, while none of the specimens should be classed as of poor quality. The presence of less than 1 per cent. of codein sulphate in morphin sulphate probably cannot modify the pharmacologic effect of the morphin to any marked extent. Probably the same may be said of the presence of 15 per cent. of narcein

hydrochlorid in narcein, as in this instance the proportion of hydrochloric acid amounts to only about 1 per cent. of the entire substance.

Based for the most part upon information compiled from the literature, but supplemented to some extent by deductions from the results obtained in the examination of the several previously-named specimens, tentative monographs for the several substances examined (except for codein phosphate and morphin sulphate, which are described in the U. S. Pharmacopeia) have been prepared. While the lists of tests in these monographs are in no sense complete, it is believed that they are adequate both for the identification of the several substances and to insure products of a sufficient degree of purity for medicinal purposes. Although the tests are tentative in nature, it was thought worth while to publish them in the hope that they might prove useful to analysts, and also, possibly, to manufacturers who may wish to prepare standards for the substances in question.

In preparing these tentative monographs an endeavor was made to select and arrange the qualitative tests so that they should be as distinctive as possible for the particular alkaloid sought. For example, narcotin, papaverin, and thebain are each precipitated by potassium ferricyanid solution, but at widely different dilutions. According to Plugge,[17] narcotin and thebain are not precipitated by this reagent from dilutions above 0.25 per cent., while papaverin may still be precipitated from dilutions of 0.025 per cent. if the solution be allowed to stand. Narcein may be precipitated from its salts by potassium ferricyanid solution as free alkaloid. Morphin and codein are not precipitated as ferricyanids even from highly-concentrated solutions. Consequently, by taking care that the alkaloidal solution be less than 0.25 per cent. in strength, papaverin alone of the six more important opium alkaloids is

17. Arch. Pharm., 1882, [3] xx, 889 et. seq.

precipitated by potassium ferricyanid as the alkaloidal ferricyanid. Again, narcotin and papaverin are the only alkaloids of the group which are precipitated in the free state by sodium acetate solution.

MONOGRAPH I—NARCEIN ($C_{23}H_{27}O_8N.3H_2O$)

Narcein occurs in fine, white, silky needles or in white prisms which may be partially effloresced to a grayish-white powder; odorless and having a slightly bitter taste, with a styptic after-taste.

Slightly soluble in water; readily soluble in hot water; slightly soluble in alcohol; readily soluble in hot alcohol; insoluble in ether; insoluble in chloroform, petroleum ether, or benzin; soluble in a warm mixture of equal parts of chloroform and isobutyl alcohol; somewhat soluble in ammonia water and in diluted potassium hydroxid solution.

At 100 C. narcein loses its water of hydration (10.8 per cent.). If exposed to the air the anhydrous alkaloid absorbs water equivalent to one molecule of water of hydration. The water of hydration in commercial narcein is variable, the quantity depending somewhat on the method of crystallization.

The melting point of narcein is variable, depending upon its content of water of hydration. Fully hydrated narcein melts at 170 C.; the anhydrous base melts at 163 C. to 165 C.; admixture with narcein hydrochlorid lowers the melting point.

A solution of narcein in hot water is neutral and is optically inactive.

If about 0.01 gm. of narcein be dissolved in 10 c.c. of water containing a few drops of hydrochloric acid, a few drops of a very weak iodin solution (about 1 in 1000) added, and the mixture shaken for several minutes, a dark blue precipitate should be produced (distinction from *other opium alkaloids*).

If about 0.01 gm. of narcein be dissolved in 10 c.c. of warm water containing a few drops of hydrochloric acid, the solution cooled, and a few drops of potassium-zinc iodid solution added, a precipitate of white, hair-

like crystals should slowly be formed; the crystals become blue on standing (distinction from *other opium alkaloids*).

If about 0.01 gm. of narcein be dissolved in 5 c.c. of water containing a few drops of hydrochlorid acid and 1 cc. of chlorin water added, followed by an excess of ammonia water, an orange-red coloration should be produced (distinction from the *thebain*, which gives a reddish-brown color).

If about 0.001 gm. of narcein be dissolved in 0.1 c.c. of nitric acid a rapidly fading yellow color should be produced.

If about 0.001 gm. of narcein be dissolved in 0.1 c.c. of sulphuric acid a yellowish-brown coloration should be produced; this slowly changes to cherry red on standing; more quickly on warming.

If about 0.001 gm. of narcein be dissolved in 0.2 c.c. of sulphuric acid in which about 0.001 gm. of gallic acid has previously been dissolved, a brownish-yellow solution should be produced; on cautiously heating the solution it successively becomes green, bluish-violet, and finally dark violet.

If about 0.01 gm. of narcein be evaporated with diluted sulphuric acid on a water-bath, a violet coloration should be produced; this changes to cherry red on further heating; when cold, this yields, on the addition of a trace of nitric acid or potassium nitrate, streaks of a blue-violet color.

If about 0.001 gm. of narcein be dissolved in 0.1 c.c. of sulphuric acid which contains a trace of iodic acid, a chocolate-brown color should be produced.

If about 0.01 gm. of narcotin be dissolved in 1 c.c. of water containing a few drops of hydrochloric acid and a few drops of ferric chlorid solution added, a red coloration should not be produced (absence of *meconic acid or meconates*); the further addition of a few drops of potassium ferricyanid solution should not immediately produce a blue color (absence of *morphin*).

If 0.1 gm. of narcein be dissolved in 10 c.c. of water containing a few drops of hydrochloric acid, a few drops of a saturated aqueous solution of iodic acid added, and the mixture shaken with 2 c.c. of chloroform, the chloroform layer should not be colored violet (absence of *morphin*).

If 0.1 gm. of narcein be dissolved in 10 c.c. of a 5 per cent. potassium hydroxid solution, the solution shaken with several small successive portions of ether, the ether solutions combined, washed with water, and evaporated, the residue, if any, should not respond to tests for *codein, narcotin or papaverin.*

If 0.01 gm. of narcein be dissolved in 10 c.c. of water containing a few drops of hydrochloric acid the solution should not at once become turbid on the addition of barium chlorid solution (limit of *sulphates*).

If from 0.2 gm. to 0.3 gm. of narcein be weighed and the alkaloid burned, the ash should not amount to more than 0.1 per cent. of the weight taken.

If from 0.2 to 0.3 gm. of narcein be weighed, dissolved in about 25 c.c. of warm water containing a few drops of nitric acid, the solution heated, a slight excess of silver nitrate solution added, the precipitate of silver chlorid, if any, collected, dried, and weighed in the usual way, the silver chlorid found should not correspond to more than 10 per cent. of the narcein hydrochlorid in the material taken.

MONOGRAPH II—NARCOTIN ($C_{22}H_{23}O_7N$)

Narcotin occurs in colorless, shining, rhombic prisms, in long needles or in fine, white crystalline powder; odorless and tasteless; permanent in the air.

Narcotin is insoluble in water; soluble in hot alcohol, ether, chloroform, ethyl acetate, and benzene; insoluble in cold but soluble in boiling alkalin solutions.

Narcotin melts at 174 to 176 C. At higher temperatures narcotin is decomposed with evolution of ammonia.

Narcotin is levorotatory, the specific rotatory power being — 207.35° in chloroform.

If about 0.01 gm. of narcotin be dissolved in 10 c.c. of water containing a few drops of diluted hydrochloric acid and a few drops of potassium sulphocyanate solution added, a white precipitate should be produced (distinction from *many other opium alkaloids*).

If about 0.01 gm. of narcotin be dissolved in 1 c.c. of water containing a few drops of diluted hydrochloric acid, a few drops of a 10 per cent. solution of sodium salicylate added, and the mixture shaken, a white precipitate should be produced which soon collects in resin-like masses which later become crystalline (distinction from *many other opium alkaloids*).

If about 0.01 gm. of narcotin be dissolved in 10 c.c. of warm water containing a few drops of diluted hydrochloric acid, the solution cooled, and a few drops of a 25 per cent. solution of sodium acetate added, a white precipitate should be produced at once (distinction from *many other opium alkaloids*).

If about 0.01 gm. of narcotin be dissolved in 10 c.c. of water containing a few drops of diluted hydrochloric acid and a few drops of bromin water added, a yellow precipitate should be produced which dissolves on boiling; if more of the bromin solution be added in small portions and the boiling repeated after each addition, a fine rose color should be produced (distinction from *other opium alkaloids*).

If about 0.001 gm. of narcotin be dissolved in 0.1 c.c. of nitric acid a yellow color should be produced.

If about 0.001 gm. of narcotin be dissolved in 0.1 c.c. of sulphuric acid, a green-yellow color should be produced; on warming the color becomes red, and on boiling, violet.

If about 0.001 gm. of narcotin be dissolved in 0.1 c.c. of sulphuric acid which contains a trace of nitric acid a brownish-red color should be produced; this soon changes to a blood-red color which is very persistent.

If about 0.001 gm. of narcein be dissolved in 0.2 c.c. of sulphuric acid in which about 0.001 gm. of gallic

acid has previously been dissolved and the mixture heated cautiously, a green color should be produced which changes to deep blue on further heating.

If about 0.001 gm. of narcotin be dissolved in about 0.1 c.c. of sulphuric acid which contains a trace of selenious acid, a green color should be produced which changes to greenish blue, then to violet blue, then to brown, and finally to cherry red.

If about 0.001 gm. of narcotin be dissolved in 0.1 c.c. of sulphuric acid which contains a trace of iodic acid, a violet color should be produced, which immediately becomes brown and eventually cherry red (distinction from *morphin* which yields a violet color soon becoming brown, and from *codein* which yields a moss-green color changing to brown).

If 0.01 gm. of narcotin be dissolved in 10 c.c. of diluted hydrochloric acid and a few drops of ferric chlorid solution added, a red coloration should not be produced (absence of *meconic acid or meconates*); the further addition of a few drops of potassium ferricyanid solution should not immediately produce a blue color (absence of *morphin*).

If 0.1 gm. of narcotin be dissolved in 10 c.c. of water containing a few drops of diluted hydrochloric acid, a few drops of a saturated aqueous solution of iodic acid added, and the solution shaken with 2 c.c. of chloroform, the chloroform layer should not be colored violet (absence of *morphin*).

If 0.1 gm. of narcotin be shaken with 10 c.c. of a 5 per cent. solution of potassium hydroxid, the mixture allowed to stand for an hour, filtered, and 2 c.c. of ammonium chlorid solution added to the filtrate, no crystals should separate within twenty-four hours (absence of *morphin*).

If from 0.2 gm. to 0.3 gm. of narcotin be weighed, dissolved in 50 c.c. of hot water containing a few drops of hydrochloric acid, a slight excess of very dilute ammonia water added with stirring, the mixture allowed to stand over night, filtered, the filtrate shaken with several successive portions of ether, the ether

solutions combined, washed with water, and evaporated, the residue, if any, should not respond to tests for *codein*.

If 0.1 gm. of narcotin be dissolved in 5 c.c. of water containing a few drops of diluted hydrochloric acid, the solution evaporated to dryness, the residue dissolved in 40 c.c. of water, a few drops of freshly prepared potassium ferricyanid solution added, and the mixture shaken, a yellow precipitate should not form within ten minutes (limit of *papaverin*).

If 0.1 gm. of narcotin be dissolved in 10 c.c. of water containing a few drops of nitric acid, portions of the solution should not at once become turbid on the addition of barium chlorid solution (limit of *sulphates*), or of silver nitrate solution (limit of *chlorids*).

If from 0.2 gm. to 0.3 gm. of narcotin be weighed and the alkaloid burned, the ash should not exceed 0.1 per cent. of the weight taken.

If from 0.2 gm. to 0.3 gm. of narcotin be weighed, dissolved in 10 c.c. of water containing a few drops of sulphuric acid, a slight excess of ammonia water added, the mixture shaken with three successive portions of 15 c.c. each of chloroform, or a sufficient quantity to complete the extraction, the combined chloroform solutions evaporated to dryness, the residue dried to constant weight at 100 C. and weighed, the weight should indicate not less than 99.5 per cent. of narcotin.

MONOGRAPH III—NARCOTIN HYDROCHLORID ($C_{22}H_{23}O_7N.HCl$).

The hydrochlorid of the alkaloid, narcotin, containing not less than 91.5 per cent. of narcotin.

Narcotin hydrochlorid occurs in a fine, white, crystalline powder; odorless; taste bitter; permanent in the air.

Narcotin hydrochlorid is soluble in water; soluble in alcohol; soluble in chloroform; insoluble in ether; insoluble in cold, but soluble in boiling, alkaline solutions.

An aqueous solution of narcotin hydrochlorid is neutral to litmus paper and is dextrorotatory, the specific rotatory power being 43.18° at 15 C.

If added to an aqueous solution of narcotin hydrochlorid, silver nitrate solution should produce a white precipitate which is insoluble in nitric acid.

If from 0.2 gm. to 0.3 gm. of narcotin hydrochlorid be weighed, dissolved in 10 c.c. of water, a slight excess of ammonia water added, the mixture shaken with three successive portions of 15 c.c. each of chloroform, or a sufficient quantity to complete the extraction, the combined chloroform solutions washed with water, evaporated to dryness, the residue dried to constant weight at 100 C., and weighed, the weight should indicate not less than 91.5 per cent. of narcotin. The alkaloid obtained by this process should conform to the tests for identity and purity described under narcotin.

MONOGRAPH IV—PAPAVERIN HYDROCHLORID ($C_{20}H_{21}O_4N.HCl$).

The hydrochlorid of the alkaloid, papaverin, containing not less than 88 per cent. of papaverin.

Papaverin hydrochlorid occurs in a fine, white, crystalline powder or in small monoclinic plates, or in prisms; odorless and having a bitter taste; permanent in the air.

Papaverin hydrochlorid is sparingly soluble in water; soluble in alcohol; very soluble in chloroform; insoluble in ether.

An aqueous solution of papaverin hydrochlorid has an acid reaction toward litmus paper and is optically inactive.

If added to an aqueous solution of papaverin hydrochlorid, silver nitrate solution should produce a white, curdy precipitate which is insoluble in nitric acid.

If about 0.01 gm. of papaverin hydrochlorid be dissolved in 5 c.c. of water and a few drops of cadmium-potassium iodid solution added, a dense, white precipitate should be produced.

If about 0.01 gm. of papaverin hydrochlorid be dissolved in 1 c.c. of hot alcohol, 0.5 c.c. of tincture of iodin added, the mixture shaken and allowed to stand, reddish-brown, crystalline needles of papaverin periodid should gradually appear.

If about 0.01 gm. of papaverin hydrochlorid be dissolved in 10 c.c. of water and a few drops of potassium ferricyanid solution added, a lemon-yellow precipitate of papaverin ferricyanid should form at once (distinction from the *salts of other opium alkaloids*).

If about 0.01 gm. of papaverin hydrochlorid be dissolved in 10 c.c. of water and a few drops of a 25 per cent. solution of sodium acetate added, a white precipitate should be produced at once (distinction from the *salts of many other opium alkaloids*).

If about 0.01 gm. of papaverin hydrochlorid be dissolved in a hot solution of 0.04 gm. of oxalic acid in 5 c.c. of water, the solution cooled and agitated for some time, small, short, opaque prisms of papaverin acid oxalate should form after standing (distinction from the *salts of other opium alkaloids*).

If about 0.01 gm. of papaverin hydrochlorid be dissolved in 5 c.c. of water and a few drops of platinum chlorid solution added, a pale yellow, amorphous precipitate should immediately be produced. This soon crystallizes into lance-shaped prisms, many of which are arranged in rosettes and tree-like forms (distinction from the *salts of other opium alkaloids*).

If about 0.01 gm. of papaverin hydrochlorid be dissolved in 0.1 c.c. of sulphuric acid in which a trace of iodic acid has previously been dissolved, a purple color should be produced which almost immediately becomes streaked with brown.

If about 0.001 gm. of papaverin hydrochlorid be dissolved in 0.1 c.c. of sulphuric acid containing in each c.c. one drop of formaldehyd solution, a colorless solution, or at most a faintly yellowish-green color, should be produced; this gradually changes to a deep rose, which lasts for some time, the mixture

finally becoming brown (distinction from the *salts of morphin and its esters*, which immediately give purple or violet colors).

If about 0.001 gm. of papaverin hydrochlorid be intimately mixed with about 0.001 gm. of finely-powdered potassium ferricyanid and the mixture dissolved in 0.2 c.c. of sulphuric acid containing in each c.c. one drop of formaldehyd solution, a light blue or greenish-blue color should be produced at once; this gradually changes successively to deep blue, violet blue (or bluish violet), emerald green and finally pale brownish yellow (distinction from *other opium alkaloids*). Certain other oxidizing agents, such as ammonium vanadate, cerium oxid, potassium permanganate, selenious acid, and sodium ortho-arsenate, also give the reaction with slight individual variations in the shades of color produced.

If 0.01 gm. of papaverin hydrochlorid be dissolved in 0.1 c.c. of sulphuric acid, the solution should not be colored more than very faintly pinkish or brownish (limit of the *salts of cryptopin, thebain, etc., or of other organic impurities*).

If 0.1 gm. of papaverin hydrochlorid be dissolved in 10 c.c. of water and a few drops of ferric chlorid solution added, a red coloration should not be produced (absence of *meconic acid or meconates*).

If 0.1 gm. of papaverin hydrochlorid be shaken with 10 c.c. of a 5 per cent. solution of potassium hydroxid, the mixture allowed to stand for an hour, filtered, and 2 c.c. of ammonium chlorid solution added to the filtrate, no crystals should separate within twenty-four hours (absence of *morphin salts*).

If 0.1 gm. of papaverin hydrochlorid be dissolved in 10 c.c. of water, a few drops of a saturated aqueous solution of iodic acid added, and the mixture shaken with 2 c.c. of chloroform, the chloroform layer should not be colored violet (absence of *morphin salts*).

If from 0.2 gm. to 0.3 gm. of papaverin hydrochlorid be weighed, dissolved in 50 c.c. of hot water, a slight

excess of very dilute ammonia water added with stirring, the mixture allowed to stand over night, filtered, the filtrate shaken with several successive portions of ether, the ether solutions combined, washed with water, and evaporated, the residue if any, should not respond to tests for *codein*.

If 0.1 gm. of papaverin hydrochlorid be dissolved in 10 c.c. of water and a few drops of hydrochloric acid added, the solution should not at once become turbid on the addition of a few drops of barium chlorid solution (limit of *sulphates*).

If from 0.2 gm. to 0.3 gm. of papaverin hydrochlorid be weighed and the salt burned, the ash should not exceed 0.1 per cent. of the weight taken.

If from 0.2 gm. to 0.3 gm. of papaverin hydrochlorid be weighed, dissolved in 20 c.c. of warm water, the solution cooled, a slight excess of ammonia water added, and the mixture shaken with three successive portions of 25 c.c. each of ether, or a sufficient quantity to complete the extraction, the ether solutions combined, washed with water, evaporated to dryness, the residue dried to constant weight at 100 C. and weighed, the weight should indicate not less than 88 per cent. of papaverin. The alkaloid obtained by this process should melt between 146.5 and 147.5 C.

If from 0.2 gm. to 0.3 gm. of papaverin hydrochlorid be weighed, dissolved in 20 c.c. of warm water, the solution cooled, a few drops of diluted hydrochloric acid added, 1 c.c. of freshly prepared potassium ferricyanid solution added, the mixture agitated, allowed to stand over night, filtered, the filtrate made alkaline with ammonia water, shaken with several successive portions of ether, the ether solutions combined, washed with water, evaporated, the residue dried at 100 C. and weighed, the weight should not amount to more than 2 per cent. of the weight taken (limit of the *salts of foreign opium alkaloids*).

MONOGRAPH V—THEBAIN HYDROCHLORID
($C_{19}H_{21}O_3N.HCl.H_2O$)

The hydrochlorid of the alkaloid, thebain, containing not less than 84.5 per cent. of thebain.

Thebain hydrochlorid occurs in colorless, or very faintly yellowish, rhombic prisms; odorless; taste acrid and styptic; permanent in the air.

Thebain hydrochlorid is soluble in water; soluble in alcohol; very soluble in chloroform; insoluble in ether.

At 110 C. thebain hydrochlorid loses its water of hydration (4.9 per cent.) with slight decomposition. At 100 C. in a vacuum the salt becomes anhydrous without decomposition. If exposed to the air the anhydrous salt absorbs water equivalent to one molecule of water of hydration.

An aqueous solution of thebain hydrochlorid is neutral to litmus paper and is levorotatory, the specific rotatory power being — 168.32°.

If added to an aqueous solution of thebain hydrochlorid, silver nitrate should produce a white, curdy precipitate which is insoluble in nitric acid.

If about 0.01 gm. of thebain hydrochlorid be dissolved in 5 c.c. of water and a few drops of a 10 per cent. solution of sodium salicylate added, a white, voluminous precipitate of thebain salicylate should be produced (distinction from the *salts of many other opium alkaloids*).

If about 0.01 gm. of thebain hydrochlorid be dissolved in 5 c.c. of water and 1 c.c. of chlorin water added, followed by an excess of ammonia water, a reddish-brown color should be produced (distinction from *narcein salts*, which give an orange-red color).

If about 0.001 gm. of thebain hydrochlorid be dissolved in 0.1 c.c. of nitric acid, a yellow color should be produced.

If about 0.001 gm. of thebain hydrochlorid be dissolved in 0.1 c.c. of hydrochloric acid, an orange-yellow color should be produced.

If about 0.001 gm. of thebain hydrochlorid be dissolved in 0.1 c.c. of sulphuric acid, a blood-red color should be produced; on warming this changes to orange yellow and eventually to olive green (distinction from the *salts of other opium alkaloids*).

APPENDIX 1.—THE OPIUM ALKALOIDS AND THE APPROXIMATE PERCENTAGES IN WHICH THEY OCCUR IN SMYRNA OPIUM[18]

Name	Formula	Approximate Percentage in Smyrna Opium
Morphin	$C_{17}H_{19}O_3N$	9.00–10.00
Narcotin	$C_{22}H_{23}O_7N$	5.00
Papaverin	$C_{20}H_{21}O_4N$	0.80
Thebain	$C_{19}H_{21}O_3N$	0.40
Codein	$C_{18}H_{21}O_3N$	0.30–0.4
Narcein	$C_{23}H_{27}O_8N$	0.20
Cryptopin	$C_{21}H_{23}O_5N$	0.08
Pseudo-morphin	$(C_{17}H_{18}O_3N)_2$	0.02
Laudanin	$C_{20}H_{25}O_4N$	0.01
Lanthopin	$C_{23}H_{25}O_4N$	0.006
Protopin	$C_{20}H_{19}O_5N$	0.003
Codamin	$C_{20}H_{25}O_4N$	0.002
Tritopin	$(C_{21}H_{27}O_3N)_2O$	0.0015
Laudanosin	$C_{21}H_{27}O_4N$	0.0008
Gnoscopin (*dl*-narcotin)	$C_{22}H_{23}O_7N$	Traces
Hydrocotarnin[19]	$C_{12}H_{15}O_3N$	Traces
Hydroxy-codein	$C_{18}H_{21}O_4N$	Traces
Laudanidin	$C_{20}H_{25}O_4N$	Traces
Meconidin	$C_{21}H_{23}O_4N$	Traces
Oxynarcotin	$C_{22}H_{23}O_8N$	Traces
Papaveramin	$C_{21}H_{25}O_5N$	Traces
Proto-papaverin	$C_{19}H_{19}O_4N$	Traces
Pseudo-papaverin	$C_{21}H_{21}O_4N$	Traces
Rheadin	$C_{21}H_{21}O_5N$	Traces
Xanthalin (papaveraldin)[19]	$C_{20}H_{19}O_5N$	Traces

18. Henry, "The Plant Alkaloids," 1913, p. 199.

19. These are possibly decomposition products of narcotin and papaverin, respectively.

If 0.1 gm. of thebain hydrochlorid be dissolved in 10 c.c. of water and a few drops of ferric chlorid solution added, a red coloration should not be produced (absence of *meconic acid or meconates*); the further addition of a few drops of potassium ferricyanid solution should not immediately produce a blue color (absence of *morphin salts*).

If 0.1 gm. of thebain hydrochlorid be dissolved in 10 c.c. of water, a few drops of a saturated, aqueous solution of iodic acid added, and the mixture shaken with 2 c.c. of chloroform, the chloroform layer should not be colored violet (absence of *morphin salts*).

If 0.1 gm. of finely powdered thebain hydrochlorid be shaken with 10 c.c. of a 5 per cent. solution of potassium hydroxid, the mixture allowed to stand for an hour, filtered, and 2 c.c. of ammonium chlorid solution added to the filtrate, no crystals should separate within 24 hours (absence of *morphin salts*).

If 0.1 gm. of thebain hydrochlorid be dissolved in 40 c.c. of water, a few drops of freshly prepared potassium ferricyanid solution added, and the mixture shaken, a yellow precipitate should not form within 10 minutes (limit of *papaverin salts.*)

If 0.1 gm. of thebain hydrochlorid be dissolved in 10 c.c. of water and a few drops of hydrochlorid acid added, the solution should not at once become turbid on the addition of barium chlorid solution (limit of *sulphate*).

If from 0.2 gm. to 0.3 gm. of thebain hydrochlorid be weighed and the salt burned, the ash should not exceed 0.1 per cent. of the weight taken.

If from 0.2 gm. to 0.3 gm. of thebain hydrochlorid be weighed, dissolved in 25 c.c. of water, a slight excess of ammonia water added, the mixture shaken with three successive portions of 25 c.c. each of ether, or a sufficient quantity to complete the extraction, the combined ether solutions washed with water, evaporated the residue dried to constant weight at 100 C. and weighed, the weight found should correspond to not less than 84.5 per cent. of anhydrous thebain. The alkaloid obtained by this process should melt at 192.5 C. to 193.5 C.

APPENDIX 2.—COLOR REACTIONS OF SOME OF THE OPIUM BASES

Alkaloid	Nitric Acid (sp. gr. 1.42)	Sulphuric Acid	Sulphuric Acid Plus Dilute Nitric Acid; Erdman's Reagent	Sulphuric Acid Plus Formaldehyd; Marquis' Reagent	Sulphuric Acid Plus Iodic Acid; Peroni's Reagent	Sulphuric Acid Plus Molybdic Acid; Frohde's Reagent	Sulphuric Acid Plus Selenious Acid; Laton's Reagent	Sulphuric Acid Plus Vanadic Acid; Mandelin's Reagent
Codein	Yellow, not changing to red	No color or faint transient pinkish; dirty brownish green on heating	Blue on warming	Violet; cherry red on long standing	Moss green, changing to slate; finally orange	Dirty green changing to blue and pale yellow	Green, changing to blue; then slowly to grass green	Pale green; gradually changes to blue
Morphin.....	Orange red, turning yellow on heating	Cold, no color or faint pink; on heating, variable	Orange brown	Intense purple...	Violet, soon becoming brown	Intense purple; yellow and blue streaks or zones; finally green	Blue, changing to green; then to brown	Bluish violet, slowly becoming dark brown
Narcein....	Yellow, rapidly fading	Brown, dissolving to yellow solution; changing to dark red on warming	Brown yellow, becoming mahogany brown on heating	Yellowish brown, soon becoming brown; green after some time	Chocolate brown	Brownish green changing to yellow and reddish yellow brown to blue	Light brown.....	Brown, changing to bluish violet; finally reddish brown
Narcotin...	Yellow	Darkens, on gentle heating, to orange and brick red; violet, on boiling	On warming, pink, changing to blood red	Fugitive purple; pale violet, soon fading to slate; then orange with red zones; finally brown	Reddish brown and eventually cherry red	Yellowish green, changing to green with blue streaks or zones; finally blue	Green, changing to greenish blue; violet blue; then brown and finally cherry red	Orange, changing to red
Papaverin....	Yellow	No color if pure; violet on heating	No color if pure	Yellowish green; deep rose and finally brown	Purple; immediately becomes streaked with brown	No color if pure	Pale green, changing to greenish blue; olive green; chocolate	Pale green; slowly changing to a bluish violet
Thebain.....	Yellow	Blood red, turning orange yellow; olive green on heating	Orange red.	Red	Red	Blood red, turning orange yellow and colorless	Blood red.....	Red

ANALYSIS OF EPILEPSY NOSTRUMS IN REFERENCE TO THE BROMID AND CHLORID CONTENT

Paul Nicholas Leech, Ph.D.

A study of a series of epilepsy "cures" was undertaken in order to determine the relative composition of these nostrums, especially in reference to the amounts of ammonium, potassium and sodium bromids and chlorids present. Except in the case of quantitative determination of bromin and chlorin, no original methods have been worked out. A general scheme has been devised, however, and it is thought to be not without interest to many that this scheme be published.

Alkaloid, alcohol, ammonium, calcium, potassium, sodium, chlorid and bromid determinations are described.

1. Alkaloids.—Twenty c.c. of the original solution was placed in a separatory funnel, diluted, acidified and shaken with chloroform. A heavy emulsion would generally form, which was broken up by allowing the contents of the flask to stand about five minutes, then pouring the solution onto a vacuum filter. (This filter was made by placing a platinum cone in an ordinary funnel, and packing the cone with cotton, which was then saturated with chloroform.) The filter was washed well. If necessary, the process was repeated until the emulsion was no more. The filtrate was transferred, with rinsing, to a separatory funnel, the chloroform layer drawn off, and the aqueous solution shaken with another portion of chloroform. After the removal of the chloroform, the aqueous layer was then made ammoniacal, and shaken with several portions of chloroform. The combined chloroform extracts were transferred to another funnel, shaken with acidified water and the chloroform drawn off. The aqueous solution was made ammoniacal, and the alkaloid content shaken out with chloroform. The chloroform extract was evaporated in a tared dish, the residue dried and weighed.

2. Alcohol.—Fifty c.c. of the original was diluted to about 130 or 150 c.c., and the alcohol distilled off, the distillate being made up to 100 c.c. according to the "Official and Provisional Method of Analysis," U. S. Department of Agriculture, page 83. Sometimes it was necessary to distill first from a slightly acid solution, then make the distillate slightly alkaline and redistill. In one or two cases, the distillate had to be saturated with salt and shaken with ligroin owing to the presence of volatile oil. The aqueous solution was again distilled.

3. Ammonia.—Ten c.c. of the original solution was transferred into the flask of a Kjeldahl distillation apparatus. A pinch of granulated zinc, water and sodium hydroxid were added. The ammonia was distilled into 25 c.c. of normal hydrochloric acid, the adapter of the condenser being well immersed in the standard acid solution. The acid was titrated with sodium hydroxid, methyl orange being used as indicator, and the amount of ammonia there calculated.

4. Calcium.—If calcium was present, 25 c.c. of the original was delivered into a beaker and then filtered. The beaker and filter were washed well. The filtrate was diluted to suitable volume, made ammoniacal, and with gentle boiling, ammonium oxalate was added. The calcium oxalate was filtered off (on paper); the filtrate and washings made up to exactly 250 c.c. at 15 C. The filtrate was used for the potassium and sodium determinations. The precipitate was dried, heated and ignited to constant weight in a platinum dish. (Quantitative determinations on calcium solutions of known strength demonstrated that, if the process was carried out in the presence of glycerin or sugar, there was no appreciable error.)

5. Sodium and Potassium.—If calcium was present, the filtrate described in the preceding paragraph was employed. If not, 25 c.c. of the original was delivered into a 250 c.c. volumetric flask and diluted up to the mark. Twenty-five c.c. of one of the above-described solutions was pipetted into a platinum dish containing 4 c.c. of sulphuric acid. The dish was placed on a steam bath, allowed to remain for several hours, then removed to a three-heat electric stove and the temperature so controlled so that the sulphuric acid slowly evaporated, but did not fume copiously. (This point is the most difficult in the entire analysis. The liquid cannot be evaporated to dryness and then ignited or charred, owing to the volatility of the bromids. On the other hand, with a large amount of organic matter, as in syrups, it is hard to heat the sulphuric acid mixture without loss.) As soon as the sulphuric acid was entirely, or almost, evaporated, the dish was cautiously heated with a flame. After the contents had reached a dull red heat, the flame was removed. One or 2 c.c. of sulphuric acid was added, and the whole carefully heated to ignition. This treatment was repeated until the carbon had been entirely oxidized. The dried residue was treated with two drops of sulphuric acid and carefully ignited. After cooling in a desiccator, the contents (sodium and potassium sulphate) were weighed.

In order to determine the potassium, the sulphates were dissolved in water and transferred to a Jena beaker. A calculated excess of chlor-platinic acid was added, and the whole evaporated to a syrupy consistency. This was treated with an 80 per cent. alcoholic solution and the precipitated potassium chlor-platinate, with some sodium sulphate, was filtered and washed well with alcohol. The filter paper was pierced, and the residue was washed into a beaker by the aid of a stream of water. The filtrate was acidified with hydrochloric acid, the whole diluted to 100 or 150 c.c., and heated to boiling in order to dissolve the potassium platinum salt. After cooling for about fifteen minutes, granulated zinc[1] was carefully added (a watch-glass cover must be on the beaker to prevent loss by spattering) until all the platinum had been reduced. The zinc must also be entirely in solution. The metallic platinum was thrown onto a tared platinum Gooch crucible, washed well, ignited and weighed. The weight of the platinum times the factor 0.4006 gives the equivalent weight of the potassium. The factor 0.8927 converts the weight of the platinum to potassium sulphate.

6. Bromid and Chlorid.—The bromid and chlorid determinations were made (1) by the indirect method of adding an excess of silver nitrate to a known amount of the sample, then weighing the combined silver bromid and silver chlorid. The excess of silver in the filtrate is determined either gravimetrically or volumetrically. In these experiments the excess was weighed as silver chlorid. This method served as a check on the second. 2. The second method differed essentially in that the combined silver bromid and silver chlorid precipitate was dissolved in strong (about 28 per cent.) ammonium hydroxid solution, the silver then being precipitated and weighed as silver iodid.

Method 1

Twenty-five c.c. of the original was made up to exactly 250 c.c. Of this solution (1:10), 25 c.c. was delivered into a 250 c.c. Erlenmeyer flask, diluted with water and acidified with nitric acid. Fifty c.c. of fifth-normal silver nitrate solution was pipetted into the flask. The flask was stoppered, shaken and the silver precipitate allowed to settle. The supernatant liquid was decanted through a weighed Gooch filter, with vacuum. (A 500 c.c. Erlenmeyer flask was placed

1. Zinc must be tested to prove absence of lead.

in a vacuum bell jar desiccator and the filtrate delivered into this flask.) After repeating a couple of times this shaking with water and acid, the whole precipitate was brought onto the Gooch crucible and washed well. The precipitate (combined silver bromid and silver chlorid) was dried for three hours at 120°, then weighed. The silver in the filtrate was precipitated as the chlorid, and after treatment of washing, similar to above, the precipitate was thrown onto a weighed Gooch crucible, dried and weighed. The amount of silver bromid and silver chlorid was calculated according to the following equations:

w = wt. of combined AgBr and AgCl.
x = wt. of AgBr.
(w-x) = wt. of AgCl.
k = wt. of Ag. in standard silver nitrate used.
a = wt. of AgCl from excess of silver nitrate.

$$.7527\ (w-x) + .5744\ x = k - .7527w$$

or transposing

$$.1783\ x = .7525\ (w + a) - k.$$

From the silver bromid and silver chlorid, the amounts, in the original, of bromin and chlorin can be readily calculated.

Method 2

This method consists of two distinct operations, A and B.

A. The weight of the combined silver bromid and chlorid precipitate from 25 c.c. of the solution (25 c.c. to 250 c.c.) was determined in same manner as above, except that standard silver solution need not be used.

B. Twenty-five c.c. of the same solution as used in A was placed in a 250 c.c. Erlenmeyer flask, treated with sufficient silver nitrate, and shaken with water and some nitric acid. The supernatant liquid was decanted through a vacuum filter (consisting of an ordinary funnel, with platinum cone and filter paper). No more precipitate than possible, however, was allowed to leave the flask. After washing, the filter was removed from the suction flask onto a filter stand, and arranged so as to deliver into the flask containing the silver precipitate. Enough strong (about 28 per cent.) ammonium hydroxid solution was poured through the filter into the flask so that, after agitation, the silver salts were completely dissolved. A calculated excess of potassium iodid solution was added to the solution of the complex silver ammonia compounds, which precipitated silver iodid, and the flask with contents was heated on a steam bath for several hours. After

cooling, the liquid was decanted through a tared Gooch filter, the residue washed with water by shaking the contents in the stoppered flask, and again decanting through the Gooch filter. The next two washings were made with a dilute nitric acid solution, then the whole of the precipitate brought on the Gooch, dried and weighed. This weight of silver iodid represented the amount of silver which was formerly present as silver bromid and silver chlorid.

$$
\begin{aligned}
w &= \text{wt. of AgCl and AgBr.} \\
x &= \text{wt. of AgBr.} \\
(w\text{-}x) &= \text{wt. of AgCl.} \\
p &= \text{wt. of AgI.} \\
0.7527\ (w\text{-}x) &\pm .5744\ x = .4597\ p. \\
1783\ x &= .7527\ w - .4597\ p.
\end{aligned}
$$

COMPARISON OF THE TWO METHODS ON SEVERAL CHLORID AND BROMID DETERMINATIONS

	Method 1		Method 2	
	Bromin	Chlorin	Bromin	Chlorin
	%	%	%	%
1	13.28	0.05	13.18	0.04
2	13.30	0.06	13.21	0.08
3	10.89	0.17	10.77	0.24
4	16.07	0.29	16.25	0.13
5	16.13	0.14	16.25	0.13
6	15.14	0.05	15.18	0.03
7	6.12	0.82	6.15	0.80
8	6.13	0.62	6.18	0.78

The advantages of the second method are (1) that it is not necessary to have a standard silver nitrate solution, nor are there any errors from incorrect standardization; and (2) that the weight of silver iodid is larger than the weight of the combined precipitates, whereas the weight of the silver chlorid, due to excess of silver nitrate, is generally less than the weight of the combined precipitate. The weight of silver iodid being larger, the percentage of error is less.

The following epilepsy "remedies" were discussed in THE JOURNAL of the American Medical Association at various dates.

Peebles' Epilepsy Cure

Of this THE JOURNAL[1] said:

"Peebles' epilepsy cure is put out by the Dr. Peebles Institute of Health, Ltd., Battle Creek, Mich. This company has for its chairman, J. M. Peebles, M.D., and for its treasurer and general manager, W. T. Bobo, M.D.

1. THE JOURNAL A. M. A., Jan. 30, 1915, p. 455.

"The Peebles' Institute reaches its victims in the usual manner: advertisements in not-too-particular newspapers and magazines. A 'free trial treatment' and a booklet containing much 'scare' material forms part of the bait. In common with practically all 'epilepsy cures' the Peebles' Institute leads the public to believe that it does not use those drugs commonly prescribed by physicians in such cases. Also in common with its kind, the concern does actually use bromids."

The Peebles' Epilepsy Treatment was submitted to the Chemical Laboratory for examination. The treatment consisted of two original bottles, labeled, respectively, No. 1 and No. 2.

Peebles epilepsy cure. Peebles received his diploma from a low grade medical school (now extinct) after he was fifty years old. In addition to being president of an "epilepsy-cure" concern, he sells a book opposing vaccination.

Peebles' Epilepsy Treatment No. 1.—The bottle of "Peebles' Epilepsy Treatment No. 1" contained 350 c.c. (12 fluidounces) of a brown liquid with extractive matter present and had an odor resembling celery and valerian. The liquid seemed to consist mainly of a hydro-alcoholic solution of extractives with flavoring. The specific gravity at 15.6 C. was 1.1040. The solid residue weighed 29.4 per cent. and the ash weighed 1.17 per cent. Quantitative determination showed 11.40 per cent. absolute alcohol by volume. The dose is 1 teaspoonful at mealtime.

Peebles' Epilepsy Treatment No. 2.—The bottle of "Peebles' Epilepsy Treatment No. 2" contained about 350 c.c. (12 fluid-ounces) of a brown liquid, having extractive matter present and a valerian-like odor. The specific gravity at 15.6 C. was 1.1601. Qualitative tests demonstrated the presence of alcohol, ammonium, potassium, sodium (traces), bromid and chlorid. Quantitative determinations yielded the following:

Alcohol (by volume)	8.44 per cent.
Ammonia (NH_3) (by weight)	1.09 per cent.
Potassium (K^+) (by weight)	5.06 per cent.
Sodium (Na^+) (by weight)	0.01 per cent.
Bromid (Br^-) (by weight)	15.18 per cent.
Chlorid (Cl^-) (by weight)	0.03 per cent.

Essentially, each 100 c.c. of the solution contains 7.3 gm. of ammonium bromid and 17.9 gm. of potassium bromid. Calculating from the bromid determination, each dose, one teaspoonful (1 fluidram), contains the equivalent of 16.8 grains of potassium bromid, and each daily dose (three teaspoonfuls) corresponds to 50.4 grains of potassium bromid.

THE JOURNAL concluded as follows:

"The report shows, as might have been expected, that the Peebles epilepsy treatment consists, essentially, in giving bromids. . . . There is no justification for selling to epileptics, bromid-containing nostrums bearing no hint of the presence of such drugs and without warning of their powerful and dangerous character. The indiscriminate use of bromids is dangerous."

Details of Analysis

No. 1

Alcohol.—The specific gravity of the 100 c.c. distillate was 0.99188 at 15.6 C. The alcohol was distilled from 50 c.c. of the original solution. This is equivalent to 11.40 per cent. alcohol by volume.

Residue and Ash.—The residue from 25 c.c. of the original weighed 8.112 gm. and the ash weighed 0.325 gm. This is equivalent to 29.4 per cent. of residue and 1.17 per cent. of ash by weight.

No. 2

Alcohol.—The specific gravity of the 100 c.c. distillate was 0.99392 at 15.6 C. The alcohol was distilled from 50 c.c. of the original. This is equivalent to 8.44 per cent. of alcohol by volume.

Ammonia.—(*a*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 7.86 c.c. of normal hydrochloric acid. This is equivalent to 1.33 gm. of ammonia in

100 c.c., or 1.07 per cent. (*b*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 7.57 c.c. of normal hydrochloric acid. This is equivalent to 1.28 gm. of ammonia in 100 c.c., or 1.10 per cent.

Sodium and Potassium.—(*a*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) yielded 0.3304 gm. of combined sulphates, and 0.3690 gm. of platinum. This is equivalent to 5.91 gm. of potassium and 0.01 gm. of sodium, in 100 c.c. of the original, or 5.09 per cent. of potassium and 0.01 per cent. of sodium. (*b*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) yielded 0.3254 gm. of combined sulphates and 0.3642 gm. of platinum. This is equivalent to 5.83 gm. of potassium and 0.01 gm. of sodium in 100 c.c. of the original, or 5.02 per cent. of potassium and 0.01 per cent. of sodium.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) was treated with 1.001 times fifth-normal silver nitrate. The weight of the combined (w) silver bromid and silver chlorid weighed 1.0391 gm., and the weight of the silver chlorid (a), due to the excess of silver nitrate, weighed 0.6411 gm. This is equivalent to 17.57 gm. of bromin and 0.06 gm. of sodium in 100 c.c., or 15.14 per cent. of bromin and 0.05 per cent. of chlorin. (*b*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) was treated so as to determine only the weight of the combined (w) silver bromid and silver chlorid. This weighed 1.0389 gm. (This weight was used in conjunction with above for determination according to Method B.) (*c*) Method B. (The weight of the combined silver bromid and silver chlorid from 25 c.c. of the solution (25 c.c. to 250 c.c.) was taken as the average of above.) The weight of silver iodid was 1.2986 gm. This is equivalent to 17.65 gm. of bromin and 0.02 gm. of sodium in 100 c.c., or 15.20 per cent. of bromin and 0.02 per cent. of sodium. (*d*) The weight of silver iodid was 1.7995 gm. This is equivalent to 17.62 gm. of bromin and 0.03 gm. of sodium in 100 c.c., or 15.18 per cent. of bromin and 0.03 per cent. of chlorin.

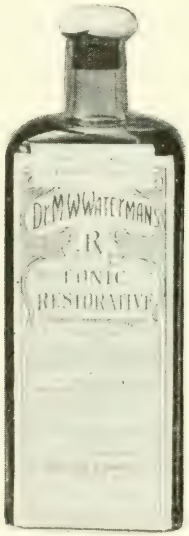
Waterman's Tonic Restorative

THE JOURNAL commented as follows[2] on this preparation:

"The Waterman Institute of New York is one of the names under which Alexander W. Chappell has advertised 'cures' for epilepsy and for the morphin habit. Chappell, who is said to be in the real estate business at Red Bank, N. J., also has operated under the name of the Lexington Drug and Chemical Company, which put out the Waterman 'epilepsy cure.'

2. THE JOURNAL A. M. A., March 6, 1915, p. 847.

"Apparently, it is not from New York alone that Chappell carries on his business. Newspaper advertisements identical in general appearance and wording with those of the Waterman Institute 'news items' have been published telling of the marvelous results alleged to have been achieved in the treatment of epilepsy by one Dr. H. W. Perkins of Red Bank, N. J. Perkins apparently acts for Chappell both under his own name and also under the name of the Dr. R. H. Kline Company, a nostrum concern having the same address as the Lexington Drug and Chemical Company and, like it, said to be owned or controlled by A. W. Chappell."



Dr. M. W. Waterman's Tonic Restorative, a so-called epilepsy "cure."

One original bottle of "Dr. Waterman's Restorative," manufactured by Lexington Drug and Chemical Co., New York, N. Y., was submitted to the Chemical Laboratory for examination.

The bottle contained about 350 c.c. (11½ fluidounces) of a brown liquid, having extractive matter present and with an odor of cinnamon. The specific gravity at 15.6 C. was 1.1788. Qualitative tests demonstrated the presence of cin-

chona alkaloids, ammonium, potassium, sodium, chlorid and bromid. Quantitative determinations yielded the following:

Alkaloids (by weight)	0.04 per cent.
Ammonia (NH_3) (by weight)	1.30 per cent.
Potassium (K^+) (by weight)	2.70 per cent.
Sodium (Na^+) (by weight)	1.51 per cent.
Bromid (Br^-) (by weight)	16.36 per cent.
Chlorid (Cl^-) (by weight)	0.34 per cent.

Essentially, each 100 c.c. of the solution contains approximately 8.8 gm. ammonium bromid, 9.7 gm. potassium bromid and 8.1 gm. sodium bromid. Calculating from the bromid determination, each meal-time dose, one teaspoonful (1 fluidram), contains the equivalent of 17.6 grains potassium bromid, and each daily dose (5 teaspoonfuls) corresponds to 88.0 grains of potassium bromid.

THE JOURNAL commented as follows:

"The directions on every bottle of 'Dr. M. W. Waterman's Tonic Restorative' give the following dosage for adults:

"One teaspoonful after each meal and two at bedtime, in a wineglassful or more of water."

As the chemists' report shows, these five teaspoonfuls of the Waterman nostrum contain the equivalent of 88 grains of potassium bromid. As in all 'epilepsy cures,' the natural tendency of the person taking the Waterman nostrum is to increase the dose. . . . That the Waterman concern, in common with other exploiters of 'epilepsy cures,' cares little for the health or safety of the person using its nostrum, is indicated by the statement appearing on the label under 'Doses and Directions':

"NOTE.—If these doses are not sufficient to stop the 'Fits' and 'Spasms' increase the dose . . ."

"In other words, the Waterman Institute would leave the dosage of the nostrum entirely to the judgment of the user. And the public is not told that the stuff contains bromids, while it is assured that the preparation is 'safe.'"

Details of Analysis

Alkaloid.—Twenty-five c.c. of the original, treated as described on page 46, gave 0.0124 gm. of total alkaloids. This is equivalent to 0.049 gm. in 100 c.c. or 0.04 per cent.

Ammonia.—(*a*) Ten c.c. of the original neutralized 9.12 c.c. of normal hydrochloric acid. This is equivalent to 1.55 gm. of ammonia in 100 c.c. or 1.31 per cent. (*b*) Ten c.c. of the original neutralized 9.12 c.c. of normal hydrochloric acid. This is equivalent to 1.54 gm. of ammonia in 100 c.c. or 1.30 per cent.

Sodium and Potassium.—(*a*) Twenty-five c.c. of a solution (25 c.c. original to 250 c.c.) yielded 0.3164 gm. of combined sulphate, and 0.1994 gm. of platinum. This is equivalent to 3.19 gm. of potassium and 1.79 gm. of sodium in 100 c.c., or 2.70 per cent. of potassium and 1.51 per cent. of sodium. (*b*) Twenty-five c.c. of the above-mentioned solution yielded 0.3169 gm. of combined sulphate, and 0.1994 gm. of platinum. This is equivalent to 3.19 gm. of potassium and 1.80 gm. of sodium in 100 c.c., or 2.70 per cent. of potassium and 1.52 per cent. of sodium.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of the solution (25 c.c. original diluted to 250 c.c.) was treated with 50 c.c. of 1.001 times fifth-normal silver nitrate. The weight of the combined (w) silver bromid and silver chlorid was 1.1810 gm. and the weight of silver chlorid (a), due to excess of silver nitrate, was 0.5233 gm. This is equivalent to 19.30 gm. of bromin and 0.42 gm. of chlorin in 100 c.c. of 16.37 per cent. of bromin and 0.35 per cent. of chlorin. (*b*) Treated as described above the weight of the combined (w) silver chlorid and silver bromid was 1.1792 gm. and the weight of the silver chlorid (a), due to an excess of silver nitrate, was 0.3248 gm. This is equivalent to 19.28 gm. of bromid and 0.41 gm. of chlorid in 100 c.c. or 16.35 per cent. of bromin and 0.34 per cent. of chlorin. (*c*) Method B: The weight of the combined silver bromid and silver chlorid was taken as the average of the two above. The weight of silver iodid was 1.4809 gm. This is equivalent to 16.70 per cent. of bromin and 00.16 per cent. of chlorin. (*d*) The weight of the silver iodid was 1.4830 gm. This is equivalent to 16.66 per cent. of bromin and 00.21 per cent. of chlorin.

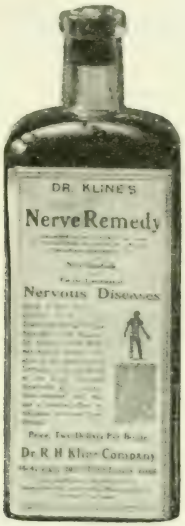
Dr. Kline's Nerve Remedy

As explained in THE JOURNAL,[3] "Dr. Kline's Epilepsy Cure used to be advertised under the name of Dr. R. H. Kline of Philadelphia. Now, it is sold by the Dr. R. H. Kline Company, 45-47 East Twentieth Street, New York—the same address as the Lexington Drug and Chemical Company, manufacturers of the Waterman 'epilepsy cure.' "

One original bottle of "Dr. Kline's Nerve Remedy," manufactured by Dr. R. H. Kline Co., New York, N. Y., was submitted to the Chemical Laboratory for examination. The bottle contained about 350 c.c. (11½ fluidounces) of a brown liquid, having extractive matter present, and with an odor

3. THE JOURNAL A. M. A., March 6, 1915, p. 848.

of cinnamon. The specific gravity of the liquid at 15.6 C. was 1.1740. Qualitative tests demonstrated the presence of cinchona alkaloids, ammonium, potassium, sodium, bromid and chlorid. Quantitative determinations yielded the following:



Another epilepsy "cure": Dr. Kline's Nerve Remedy.

Alkaloids (by weight)	0.04	per cent.
Ammonia (NH_3) (by weight)	1.29	per cent.
Potassium (K^+) (by weight)	2.57	per cent.
Sodium (Na^+) (by weight)	1.50	per cent.
Bromid (Br^-) (by weight)	16.10	per cent.
Chlorid (Cl^-) (by weight)	0.23	per cent.

Essentially, each 100 c.c. of the solution contains approximately 8.7 gm. ammonium bromid, 9.2 gm. potassium bromid and 8.0 gm. sodium bromid. Calculating from the bromid determinations each meal-time dose, one teaspoonful (1 fluidram), contains the equivalent of 17.2 grains potassium bromid, and each daily dose (5 teaspoonfuls) corresponds to 87.0 grains potassium bromid. THE JOURNAL further commented:

"The report on Dr. Kline's Nerve Remedy shows that it is identical with the product put out under the name of Dr. Waterman's Tonic Restorative. The fractional differences that appear are not more than would be found in comparing any two analyses of the same product."

Details of Analysis

Alkaloid.—Twenty c.c. of the original, treated as described on page 46, gave 0.0100 gm. of total alkaloids. This is equivalent to 0.05 gm. in 100 c.c. or 0.04 per cent.

Ammonia.—(*a*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 8.97 c.c. of normal hydrochloric acid. This is equivalent to 1.52 gm. of ammonia in 100 c.c. or 1.30 per cent. (*b*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 8.86 c.c. of normal hydrochloric acid. This is equivalent to 1.50 gm. of ammonia in 100 c.c. or 1.29 per cent.

Sodium and Potassium.—(*a*) Twenty-five c.c. of a solution (25 c.c. to 250 c.c.) yielded 0.3049 gm. of combined sulphate and 0.1897 gm. of platinum. This is equivalent to 3.03 gm. of potassium and 1.75 gm. of sodium in 100 c.c. or 2.58 per cent. of potassium and 1.48 per cent. of sodium. (*b*) Twenty-five c.c. of a solution (25 c.c. to 250 c.c.) yielded 0.3053 gm. of combined sulphates, and 0.1883 gm. of platinum. This is equivalent to 3.02 gm. of potassium and 1.50 gm. of sodium in 100 c.c. or 2.57 per cent. of potassium, and 1.50 per cent. of sodium.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of the solution (25 c.c. original diluted to 250 c.c.) was treated with 50 c.c. of 1.001 times fifth-normal silver nitrate. The weight of the combined (w) silver chlorid and silver bromid was 1.1391 gm., and the weight of silver chlorid (a), due to excess of silver nitrate was 0.5591 gm. This is equivalent to 18.87 gm. of bromin and 0.29 gm. of chlorin in 100 c.c., or 16.07 per cent. of bromin and 0.29 per cent. of chlorin. (*b*) Treated as above the weight of the combined (w) silver chlorid and silver bromid was 1.1366 gm., and the weight of the silver chlorid (*a*), due to excess of silver nitrate, was 0.625 gm. This is equivalent to 18.93 gm. of bromin and 0.23 gm. of chlorin in 100 c.c. or 16.13 per cent. of bromin and 0.19 per cent. of chlorin. (*c*) Method B: (The Weight of the combined silver bromid and silver chlorid was taken as the average above.) The weight of the silver iodid was 1.4263 gm. This is equivalent to 16.25 per cent. of bromin and 0.13 per cent. of chlorin. (*d*) The weight of the silver iodid was 1.4259 gm. This is equivalent to 16.25 per cent. of bromin and 0.13 per cent. of chlorin.

Towns' Epilepsy Treatment

Of this preparation THE JOURNAL[4] said:

"Towns' Epilepsy Treatment is marketed by the Towns' Remedy Company of Milwaukee, Wis. A few years ago this

4. THE JOURNAL A. M. A., Feb. 20, 1915, p. 683.

preparation was known as 'Dr. Towns' Epilepsy Cure' and was sold from Fond du Lac, Wis. Then came the Food and Drugs Act, which made false statements on the trade package come high, and as Towns' 'patent medicine' is not and never was 'cure' the name of the product was changed to 'Towns' Epilepsy Treatment.' The Towns concern did not move directly from Fond du Lac to Milwaukee but was for a time located at Baltimore."

One original bottle of "Towns' Epilepsy Treatment," manufactured by the Towns Remedy Co., Baltimore, was submitted to the chemical laboratory for examination. The bottle contained a brown liquid, having extractive matter

Towns' Epilepsy Treatment.

present, and with an odor of cinnamon and valerian. The specific gravity of the liquid at 15.6 C. was 1.2505. Qualitative tests demonstrated the presence of the following: Alcohol, ammonia, potassium, sodium, bromid, chlorid, iodid and sugar. Quantitative determinations yielded the following:

Alcohol (by volume)	1.00 per cent.
Ammonia (NH_3) (by weight)	1.82 per cent.
Potassium (K^+) (by weight)	2.98 per cent.
Sodium (Na^+) (by weight)	1.39 per cent.
Bromid (Br^-) (by weight)	12.81 per cent.
Chlorid (Cl^-) (by weight)	3.12 per cent.
Iodid (I^-) (by weight)	0.46 per cent.
Sugar (Sucrose) (by weight)	5.42 per cent.

Calculating from the bromid and iodid determinations, each dose, 1½ teaspoonfuls (1½ fluidrams), approximates the equivalent of 21.3 grains potassium bromid and 0.78 grain (about ¾ grain) potassium iodid. The daily dose (6 teaspoonfuls) corresponds to 85.2 grains potassium bromid and 3.12 grains potassium iodid. Considerable chlorid is also present, equivalent to approximately 6 grains sodium chlorid in 1½ teaspoonfuls, or 24 grains in the daily dose (6 teaspoonfuls).

"Evidently this 'epilepsy cure,' in common with other nostrums of the same kind, depends for its action on the presence of bromids," said THE JOURNAL. "And Towns has made the claim he 'can cure ninety-six in every hundred cases' of epilepsy!"

Details of Analysis

Alcohol.—The specific gravity of the 100 c.c. distillate was 0.99924 at 15.6 C. The alcohol was distilled from 50 c.c. of the original. The alcohol by volume was equal to 1 per cent.

Ammonia.—(*a*) Ten c.c. of the original, after the ammonia distillate treatment, neutralized 13.42 c.c. of normal hydrochloric acid. This is equivalent to 2.28 gm. of ammonia in 100 c.c. or 1.82 per cent. (*b*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 13.50 c.c. of normal hydrochloric acid. This is equivalent to 2.29 gm. of ammonia in 100 c.c. or 1.83 per cent.

Sodium and Potassium.—(*a*) Twenty-five c.c. of a solution (25 c.c. to 250 c.c.) yielded 0.3422 gm. of combined sulphate and 0.2329 gm. of platinum. This is equivalent to 3.74 gm. of potassium and 1.72 gm. of sodium in 100 c.c. or 2.99 per cent. of potassium and 1.39 per cent. of sodium. (*b*) Twenty-five c.c. of a solution (25 c.c. to 250 c.c.) yielded 0.3406 gm. of combined sulphates, and 0.2328 gm. of platinum. This is equivalent to 3.73 gm. of potassium and 1.72 gm. of sodium in 100 c.c. or 2.98 per cent. of potassium and 1.39 per cent. of sodium.

Iodid.—The iodin was determined by distilling the iodin, liberated by ferric ammonium sulphate and sulphuric acid, into potassium iodid and titrating the iodin with standard sodium thiosulphate. (*a*) Twenty-five c.c. of the solution (50 to 500 c.c.) gave iodin equivalent to 1.15 c.c. of normal thiosulphate solution. This is equivalent to 0.583 gm. of iodin in 100 c.c. or 0.46 per cent. (*b*) Twenty-five c.c. of the solution gave (50 c.c. to 500 c.c.) of iodin equivalent to 1.18 c.c. normal thiosulphate solution. This is equivalent to 0.596 gm. of iodin in 100 c.c., or 0.47 per cent.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of a solution (50 c.c. to 500 c.c.) was treated with 50 c.c. of 1.001 times fifth-normal silver nitrate. The weight of the combined silver chlorid, silver bromid and silver iodid was 1.3661 gm. Calculating from the iodin determination, the equivalent of silver iodid in the precipitate was 0.0273 gm. This makes the combined (w) weight of silver bromid, and silver chlorid equal to 1.3388 gm. The weight of silver chlorid (a), due to the excess of silver nitrate, was 0.3203 gm. This is equivalent to 16.04 gm. of bromin and 3.91 gm. of chlorin in 100 c.c. of the original, or 12.82 per cent. of bromin and 3.12 per cent. of chlorin. (*b*) Twenty-five c.c. of a solution (50 c.c. to 500 c.c.) was treated with 50 c.c. of 1.001 times fifth-normal silver nitrate. The weight of the combined silver chlorid, silver bromid and silver iodid was 1.3651 gm. Calculating from the iodin determination the equivalent of silver iodid in precipitate was 0.0273 gm. This makes the combined (w) weight of silver bromid, and silver chlorid equal to 1.3378 gm. The weight of silver chlorid (a), due to the excess of silver nitrate, was 0.3207 gm. This is equivalent to 16.01 gm. of bromin and 3.92 gm. of chlorin in 100 c.c. of the original, or 12.80 per cent. of bromin and 3.13 per cent. of chlorin.

Sugar.—Ten c.c. of the original was diluted to 100 c.c. and the direct rotation at 26 C. was found to be + 0.38°. Another 10 c.c. of the original was inverted with hydrochloric acid, cooled and diluted to 100 c.c. The rotation of the latter was found to be — 0.50° at 26 C. Calculating from these figures each 100 c.c. of the original was found to contain the equivalent of 6.78 gm. of sucrose, or 5.42 per cent.

Dr. May's Formula

THE JOURNAL[5] said of this so-called epilepsy "formula":

"W. H. May, M.D., and his so-called 'medical laboratory,' both of New York City, conduct a mail-order 'cure' for epilepsy. The nostrum, now called 'Dr. May's Formula' was, a year or so ago, 'Dr. May's Epilepticide, The Wonderful Nerve Restorer. . . .'

"Having 'discovered' the real cause of epilepsy, May naturally decided that 'the old method of 'treating Epilepsy' should be discarded. To take its place 'a *new scientific treatment* of the disease has been perfected by which have been obtained the most wonderful and marvelous cures.'"

One original bottle of "Dr. May's Formula," manufactured by Dr. W. H. May Medical Laboratory, New York, N. Y., was submitted to the Chemical Laboratory for examination.

5. THE JOURNAL A. M. A., April 3, 1915, p. 1178.

The bottle contained a brown liquid, having extractive matter present. The specific gravity of the liquid at 15.6 C. was 1.2347. Qualitative tests demonstrated the presence of alcohol, ammonia, potassium, sodium, bromid, chlorid and sucrose. Quantitative determinations yielded the following:

Alcohol (by volume)	4.50 per cent.
Ammonia (NH_3) (by weight)	0.62 per cent.
Potassium (K^+) (by weight)	0.05 per cent.
Sodium (Na^+) (by weight)	2.89 per cent.
Bromid (Br^-) (by weight)	13.29 per cent.
Chlorid (Cl^-) (by weight)	0.03 per cent.
Sugar (by weight)	1.15 per cent.

Dr. May's Formula, formerly Dr. May's Epilepticide.

Essentially each 100 c.c. of the solution contains 4.5 grams of ammonium bromid and 16.0 grams of sodium bromid. Calculating from the bromid determination, each dose, one teaspoonful (1 fluidram), contains the equivalent of 15 grains of potassium bromid, and each daily dose (4 teaspoonfuls) corresponds to 60 grains of potassium bromid.

THE JOURNAL concluded its article as follows:

"Says May of his nostrum:

"It is not poisonous; contains no narcotics — no morphin, opium, cocaine or belladonna such as are ordinarily used in other remedies for Epilepsy, and are so destructive to health."

"What are the facts? It *is* poisonous; it *does* contain a narcotic; it *is* essentially just such a mixture as is ordinarily sold as an 'epilepsy cure' and it *is* destructive of health. . . . No wonder 'patent medicine' fakers are opposed to the declaration of their formulas! It would sound the death knell of their business."

Details of Analysis

Alcohol.—The specific gravity of the 100 c.c. distillate was 0.99667 at 15.6 C. The alcohol was distilled from 50 c.c. of the original. This is equivalent to 4.50 per cent. alcohol by volume.

Ammonia.—(*a*) Fifty c.c. of the solution (25 c.c. to 250 c.c.), after the ammonia distillation treatment, neutralized 2.26 c.c. of normal hydrochloric acid. This is equivalent to 0.76 gm. of ammonia in 100 c.c., or 0.61 per cent. (*b*) Twenty c.c. original, after the ammonia distillation treatment, neutralized 9.42 c.c. of normal hydrochloric acid. This is equivalent to 0.80 gm. ammonia in 100 c.c., or 0.64 per cent.

Sodium and Potassium.—(*a*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) yielded 0.2794 gm. of combined sulphates and 0.0042 gm. of platinum. This is equivalent to 3.57 gm. sodium and 0.06 gm. potassium in 100 c.c., or 2.89 per cent. of sodium and 0.05 per cent. potassium. (*b*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) yielded 0.2745 gm. of combined sulphates and 0.0047 gm. of platinum. This is equivalent to 3.54 gm. of sodium and 0.06 gm. potassium in 100 c.c., or 2.86 per cent. sodium and 0.05 per cent. potassium.

Bromid and Chlorid.—(*a*) Twenty c.c. of the solution (25 c.c. to 250 c.c.) was treated with 1.001 times fifth-normal silver nitrate. The weight of the combined (w) silver bromid and silver chlorid was 0.7762 gm., and the weight of silver chlorid (a), due to excess of silver nitrate, was 0.1255 gm. This is equivalent to 16.40 gm. bromin and 0.06 gm. chlorin in 100 c.c., or 13.28 per cent. bromin and 0.05 per cent. chlorin. (*b*) Twenty c.c. of the solution (25 c.c. to 250 c.c.) was treated with 25 c.c. of 1.001 times fifth-normal silver nitrate solution. The weight of the combined (w) silver bromid and silver chlorid was 0.7757 gm., and the weight of the silver chlorid (a), due to excess of silver nitrate, was 0.1265 gm. This is equivalent to 16.44 gm. bromin and 0.05 gm. chlorin in 100 c.c., or 13.30 per cent. bromin and 0.04 per cent. chlorin. (*c*) Method B. (The weight of the combined silver chlorid and silver bromid from 20 c.c. of the solution (25 c.c. to 250 c.c.) was taken as the average of the above.) From 20 c.c. of the solution (25 c.c. to 250 c.c.) the silver iodid weighed 0.9722 gm. This is equivalent to 13.18 per cent. bromin and 0.04 per cent. chlorin. (*d*) The weight of silver

iodid was 0.9737 gm. This is equivalent to 13.21 per cent. bromin and 0.08 per cent. chlorin.

The Converse Treatment

This Ohio "cure" for epilepsy was commented on as follows in THE JOURNAL:[7]

"The 'Converse Treatment' for epilepsy is sold by the Converse Treatment Company of Columbus, Ohio, which is said to have for its officers Herbert E. Sanderson, president; Nathan Dawson, vice president, and Frank J. Dawson, secretary and treasurer. As is the case with most mail-

The Converse Treatment, an Ohio "cure" for epilepsy.

order medical concerns none of the individuals controlling the business seem to be physicians . . . this product was known [earlier] as the 'Converse Cure' and was put out as 'the only positive cure known, adopted and recommended by the leading physicians of the country. . . .'

"The usual warnings against all other 'cures for fits,' was part of the advertising claptrap and competitors' products were condemned under the statement that they contained 'zinc, silver or bromid, all of which but tend to aggravate the trouble in the long run.'"

Original bottles of "Converse Treatment," manufactured by the Converse Treatment Co., Columbus, Ohio, were

7. THE JOURNAL A. M. A., April 24, 1915, p. 1441.

submitted to the Chemical Laboratory for examination. Each bottle contained 165 c.c. (5½ fluidounces) of a brown liquid, having suspended extractive matter present, and with a strong odor of cinnamon. The specific gravity of the liquid at 15.6 C. was 1.1426. Qualitative tests demonstrated the presence of ammonium, calcium, sodium, potassium, chlorid and bromid. Saccharine also seemed to be present. From spectroscopic tests, lithium was not present in quantities greater than minute traces. Qualitative determinations yielded the following:

Ammonia (NH_3) (by weight).....	1.13 per cent.
Calcium (Ca^{++}) (by weight).....	0.88 per cent.
Potassium (K^+) (by weight).....	3.74 per cent.
Sodium (Na^+) (by weight).....	0.10 per cent.
Bromid (Br^-) (by weight).....	13.93 per cent.
Chlorid (Cl^-) (by weight).....	0.28 per cent.

Essentially each 100 c.c. of the solution contains about 7.3 gm. ammonium bromid, 5 gm. calcium bromid and 8.7 gm. potassium bromid. Calculating from the bromid determination, each dose 1 teaspoonful (1 fluidram) contains the equivalent of 14.5 grains of potassium bromid, or each daily dose (4 teaspoonfuls) corresponds to 58.0 gr. potassium bromid.

In concluding, THE JOURNAL remarked:

"As might have been expected from the investigation of various nostrums of the same type, the 'Converse Treatment' is but one more of the bromid mixtures. This, too, in spite of the fact that the exploiters of the stuff have in the past stated that epilepsy cures containing bromids 'tend to aggravate the trouble in the long run.'

"The statement that the Converse Treatment will cure epilepsy is as false as the other statement that the nostrum is used 'by leading physicians.' The stuff has all the limitations and dangers of a bromid mixture. It will never cure a case of epilepsy, but . . . may easily result in adding to the epileptic victim's already serious condition the dangers of bromism."

Details of Analysis

Ammonia.—(*a*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 7.64 c.c. of normal hydrochloric acid. This is equivalent to 1.29 gm. of ammonia in 100 c.c. of the original, or 1.13 per cent. (*b*) Ten c.c. of the original solution, after the ammonia distillation treatment, neutralized 7.55 c.c. of normal hydrochloric acid. This is equivalent to 1.28 gm. of ammonia in 100 c.c. of the original, or 1.12 per cent.

Calcium.—(*a*) The calcium in 25 c.c. of the original was precipitated as calcium oxalate and converted to calcium oxid. The weight of calcium oxid was 0.3535 gm. This is

equivalent to 1.009 gm. of calcium in 100 c.c., or 0.88 per cent. (*b*) The weight of the calcium oxid was 0.3537 gm. This is equivalent to 1.010 gm. in 100 c.c., or 0.88 per cent.

Sodium and Potassium.—(*a*) Twenty-five c.c. of the diluted solution (25 c.c. to 250 c.c.) yielded 0.2458 gm. of combined sulphate and 0.2742 gm. of platinum. This is equivalent to 4.38 gm. potassium and 0.015 gm. sodium in 100 c.c., or 3.82 per cent. potassium and 0.01 per cent. sodium. (*b*) Twenty-five c.c. of the diluted solution (25 c.c. to 250 c.c.) yielded 0.2465 gm. of combined sulphates, and 0.2580 gm. of potassium. This is equivalent to 4.14 gm. of potassium and 0.18 gm. sodium in 100 c.c., or 3.62 per cent. potassium and 0.16 per cent. sodium.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) was treated with 50 c.c. of fifth-normal silver nitrate (factor 1.001). The weight of the combined (w) silver bromid and silver chlorid was 0.9652 gm., and the weight of silver chlorid (a), due to an excess of silver nitrate, was 0.6911 gm. This is equivalent to 13.87 per cent. of bromin and 0.33 per cent. chlorin. (*b*) Treated as above, the weight of the combined (w) silver chlorid and silver bromid was 0.9685 gm., and the silver chlorid (a), due to excess of silver nitrate, was 0.6897 gm. This is equivalent to 13.98 per cent. of bromin and 0.22 per cent. of chlorin. (*c*) Method B. (The weight of the combined (w) silver bromid and silver chlorid was taken as the average of the foregoing.) The weight of silver iodid was 1.2113 gm. This is equivalent to 14.26 per cent. of bromin and 0.08 per cent. of chlorin. (*d*) The weight of silver iodid was 1.2135 gm. This is equivalent to 14.17 per cent. of bromin and 0.13 per cent. of chlorin.

Grant's Epilepsy Cure

Fred E. Grant, Kansas City, Mo., sells a mail-order "cure" for epilepsy. Inquiries received by THE JOURNAL A. M. A., from physicians and laymen in various widely separated parts of the United States (including points on the Atlantic and Pacific coasts), and covering a period of five or six years, led to an examination of Grant's nostrum by the laboratory. The laboratory reported:

One original bottle of a remedy for epilepsy, manufactured by Dr. Fred E. Grant, Kansas City, Mo., was submitted to the Chemical Laboratory for examination. The bottle contained 460 c.c. (about 15½ fluidounces) of a brown liquid. The specific gravity of the liquid at 15.6 C. was 1.1149. Qualitative tests demonstrated the presence of alcohol, potas-

sium, sodium, bromid and chlorid. Quantitative determinations yielded the following:

Alcohol (by volume)	1.50 per cent.
Potassium (K^+) (by weight)	4.57 per cent.
Sodium (Na^+) (by weight)	0.19 per cent.
Bromid (Br^-) (by weight)	9.76 per cent.
Chlorid (Cl^-) (by weight)	0.04 per cent.

The essential constituents of each 100 c.c. of the solution are approximately 15.8 gm. of potassium bromid and 0.9 gm. sodium bromid. Calculating from the bromid determinations, each teaspoonful (1 fluidram) contains the equivalent of 10.0 grs. potassium bromid, and each daily dose (7 teaspoonfuls) corresponds to 70.0 grs. potassium bromid.

THE JOURNAL[6] commented on these findings:

"The directions on the bottle call for Grant's cure to be given: 'Two Teaspoonfuls after Breakfast and the Noon Meal. Three Teaspoonfuls On Retiring.' This means that the victim is unknowingly taking the equivalent of 70 grains of potassium bromid daily and yet Grant has the impudent effrontery to say: 'There is nothing injurious to the system in this medicine.'"

Details of Analysis

Alcohol.—The specific gravity of the 100 c.c. distillate was 0.9988. The alcohol was distilled from 50 c.c. of the original. This is equivalent to 1.50 per cent. alcohol.

Potassium and Sodium.—(*a*) Twenty-five c.c. of the solution (50 c.c. to 500 c.c.) yielded 0.3014 gm. of combined sulphates and 0.3197 gm. of platinum. This is equivalent to 5.12 gm. potassium and 0.20 gm. sodium in 100 c.c., or 4.59 per cent potassium and 0.19 per cent. sodium. (*b*) Twenty-five c.c. of the solution (50 c.c. to 500 c.c.) yielded 0.3011 gm. of combined sulphates and 0.3172 gm. platinum. This is equivalent to 5.08 gm. potassium and 0.23 gm. sodium in 100 c.c., or 4.55 per cent. potassium and 0.20 per cent. sodium.

Bromid and Chlorid.—The combined silver bromid and silver chlorid precipitate from 25 c.c. of (50 c.c. to 500 c.c.) was weighed on a Gooch crucible. In order to determine the amount of silver, the solution (50 c.c. to 500 c.c.) was treated with silver nitrate reagent, and the chlorid and bromid precipitate transferred to a paper filter and washed well. The paper was punctured and the precipitate washed into a beaker, first by a solution containing 2 gm. of potassium cyanid, then with distilled water. The solution containing the dissolved silver salts was placed in a platinum dish and electrolyzed at room temperature, with a current of 2.8 volts

6. THE JOURNAL A. M. A., Sept. 8, 1913, p. 898.

The results of three such runs were 0.3716 gm. silver, 0.3704 gm., and 0.3700 gm., respectively, or an average of 0.3710 gm. silver. (*a*) The weight of the combined silver halid precipitate was 0.6442 gm. This calculates to 10.86 gm. bromid (Br^-) and 0.056 gm. chlorid (Cl^-) in 100 c.c. of the original. (*b*) The weight of the combined silver halid precipitate was 0.6450 gm. This calculates to 10.92 gm. bromid (Br^-) and 0.032 gm. chlorid (Cl^-) in 100 c.c. of the original. The average per cent. is 9.76 per cent. bromid (Br^-) and 0.04 per cent. chlorid (Cl^-).

Dr. Guertin's Nerve Syrup

THE JOURNAL[8] commented on this, another member of the "epilepsy cure" family, as follows:

"Dr. Guertin's Nerve Syrup is sold by a Cincinnati concern, the Kalmus Chemical Company, or, as it has been termed, the Otto Kalmus Chemical Company. Each carton of the nostrum bears a picture of an apparently well-fed but not otherwise prepossessing individual under which, in autograph style, is the name 'A. L. Guertin, M.D.'

"Kalmus' scheme was to advertise that he could cure epilepsy by remedies unknown to medical science and termed by him the 'Schönka treatment.' The government proved that his remedies were in fact the bromids with adonis vernalis, and the federal inspectors were unable to learn of any 'cures' that had been effected. They did come across some cases in which the victims had become so seriously affected by the bromids that the 'treatment' had to be discontinued and the unfortunates confined in state institutions."

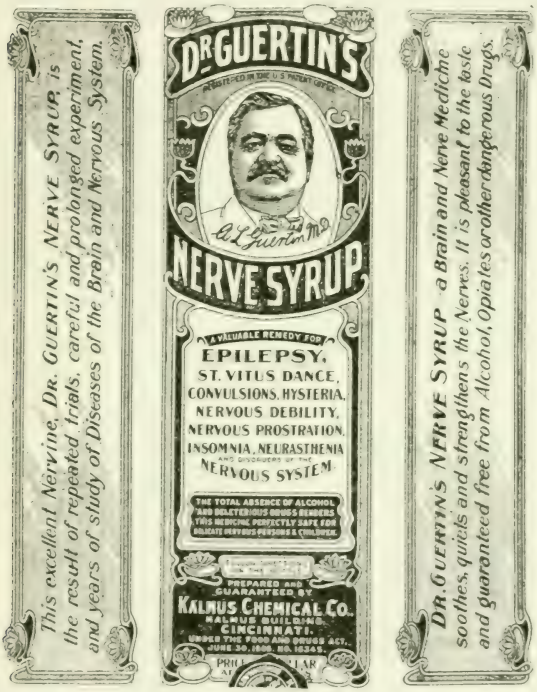
That the composition is not so very unlike that reported by the government is evidenced by the following:

One original bottle of "Dr. Guertin's Nerve Syrup," manufactured by the Kalmus Chemical Co., Cincinnati, Ohio, was submitted to the Chemical Laboratory for examination. The bottle contained 240 c.c. (8 fluidounces) of a brown syrupy liquid having extractive matter present. The specific gravity of the liquid at 15.6 C. was 1.3333. Qualitative tests demonstrated the presence of a very small amount of an alkaloid, ammonium, calcium, potassium, sodium, strontium, bromid, chlorid and sugar, a trace of invert sugar was also present. Quantitative determinations yielded the following:

Ammonia (NH_3) (by weight)	0.38 per cent.
Calcium (Ca^{++}) (by weight)	0.10 per cent.
Potassium (K^+) (by weight)	2.47 per cent.
Sodium (Na^+) (by weight)	1.00 per cent.
Strontium (Sr^{++}) (by weight)	0.40 per cent.
Bromid (Br^-) (by weight)	11.43 per cent.
Chlorid (Cl^-) (by weight)	0.20 per cent.
Sugar (Sucrose) (by weight)	34.44 per cent.

8. THE JOURNAL A. M. A., March 27, 1915, p. 1094.

Essentially each 100 c.c. of the solution contains 2.9 grams ammonium bromid, 1.5 grains strontium bromid, 0.9 grams calcium bromid, 10.9 grams potassium bromid, 4.5 grams sodium bromid, with 45.9 grams sugar. Calculating from the bromid determinations each dose, 1 to 2 teaspoonfuls (1 to 2 fluid drams) contains the equivalent of 13.9 to 27.8 grains



Reduced reproduction of Dr. Guertin's Nerve Syrup, a worthless "patent medicine" sold as a cure for epilepsy.

potassium bromid, and the daily dose (4 to 8 teaspoonfuls) corresponds to 55.6 to 111.2 grams potassium bromid.

"Bromids, of course—although the public is not appraised of the fact," said THE JOURNAL. "'Harmless' it is said to be, although it possesses all the potency for harm that resides in secret mixtures of the bromids. Dosage? Left, as usual, practically in the hands of the person who takes it:

"If the doses as given on the bottle do not bring the attacks under control, increase the quantity. . ."

"Firm in the belief that the preparation is what the exploiters claim, 'a mild and harmless nervine,' ignorant of the presence of the bromids, the sufferer is dosed into physical and mental inactivity. Such must be the inevitable result of the indiscriminate use of 'Dr. Guertin's Nerve Syrup' which is not a 'safe and dependable remedy for all nervous diseases' as claimed."

Details of Analysis

Ammonia.—(*a*) Ten c.c. of the original, after the ammonia distillation treatment, neutralized 3.03 c.c. of normal hydrochloric acid. This is equivalent to 0.51 gm. of ammonia in 100 c.c., or 0.38 per cent. (*b*) Ten c.c. of the original after the ammonia distillation treatment, neutralized 3.10 c.c. of normal hydrochloric acid. This is equivalent to 0.52 gm. ammonia in 100 c.c. or 0.39 per cent.

Calcium.—(*a*) The calcium in 25 c.c. of the original was precipitated as calcium oxalate and converted to calcium oxid. The weight of calcium oxid was 0.0439 gm. This is equivalent to 0.0140 gm. in 100 c.c. or 0.10 per cent. (*b*) The weight of calcium oxid was 0.0449 gm. This is equivalent to 0.0138 gm. in 100 c.c., or 0.11 per cent. (see *Strontium*).

Sodium and Potassium.—(*a*) Twenty-five c.c. of a solution (25 c.c. to 500 c.c.) yielded 0.1490 gm. of combined sulphate and 0.1104 gm. of platinum. This is equivalent to 3.52 gm. potassium and 1.28 gm. sodium, or 2.68 per cent. potassium and 0.98 per cent. sodium. (*b*) Twenty-five c.c. of a solution (25 c.c. to 500 c.c.) yielded 0.1545 gm. of combined sulphate and 0.1051 gm. platinum. This is equivalent to 3.68 gm. of potassium and 1.34 gm. sodium, or 2.82 per cent. potassium and 1.02 per cent. sodium.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) was treated with 50 c.c. of 1.001 times fifth-normal silver nitrate. The weight of the combined (w) silver bromid and silver chlorid was 0.9250 gm., and the weight of the silver chlorid (a), due to excess of silver nitrate was 0.7228 gm. This is equivalent to 15.24 gm. bromin and 0.28 gm. chlorin in 100 c.c., or 11.43 per cent. bromin and 0.21 per cent. chlorin. (*b*) Treated as above, the weight of the combined (w) silver bromid and silver chlorid was 0.9240 gm., and the weight of silver chlorid (a), due to excess of silver nitrate, was 0.7243 gm. This is equivalent to 15.26 gm. bromin and 0.268 gm. chlorin in 100 c.c., or 11.44 per cent. bromin and 0.20 per cent. chlorin.

Strontium.—Strontium was separated from the calcium by converting the precipitated carbonates into nitrates, then dissolving out the calcium nitrate with absolute alcohol ether. The strontium was then weighed as sulphate. (*a*) The weight of strontium sulphate ($SrSO_4$) representing 25 c.c. of the original was 0.2830 gm. This is equivalent to 0.54 gm. per 100 c.c., or 0.40 per cent. (*b*) The weight of strontium sulphate from 25 c.c. of the original was 0.2815. This is equivalent to 0.53 gm. per 100 c.c., or 0.39 per cent.

Dr. Croney's Specific for Epilepsy

Of this so-called epilepsy "cure" THE JOURNAL[9] said:

"Dr. James T. Croney of Columbus, Ohio, calls himself a 'specialist' in epilepsy. His specialty is of the mail-order variety, and he treats patients he never sees, for conditions that are self-diagnosed.

"Of the 'treatment,' Croney says:

". . . the key to my success is due to the fact that I have dissected epilepsy — so to speak — and have prepared a remedy that opposes it at all times."

One bottle of "Dr. Croney's Specific for Epilepsy," manufactured by J. T. Croney, Columbus, Ohio, was submitted to the Chemical Laboratory for examination. The bottle contained 980 c.c. (32⅔ fluidounces) of a brown liquid, having extractive matter present. The specific gravity of the liquid at 15.6 C. was 1.1403. Qualitative tests demonstrated a trace of alkaloid, alcohol, ammonia, sodium, potassium, carbonate, chlorid and bromid. A resin was also present. The liquid was distinctly alkaline. Quantitative determinations yielded the following:

Alcohol (by volume)	3.70 per cent.
Ammonia (NH_3) (by weight)	0.46 per cent.
Potassium (K^+) (by weight)	5.02 per cent.
Sodium (Na^+) (by weight)	0.04 per cent.
Carbonate ($CO_3=$) (by weight)	0.98 per cent.
Bromid (Br^-) (by weight)	10.91 per cent.
Chlorid (Cl^-) (by weight)	0.16 per cent.
Resinous material (by weight)	0.47 per cent.

Essentially each 100 c.c. of the solution contains approximately 3.0 gm. ammonium bromid and 16.1 gm. potassium bromid. Calculating from the bromid determination, each dose, 2 teaspoonfuls (2 fluidrams) contains the equivalent of 16.9 grains potassium bromid, or the daily dose (6 teaspoonfuls) correspond to 50.7 grains potassium bromid.

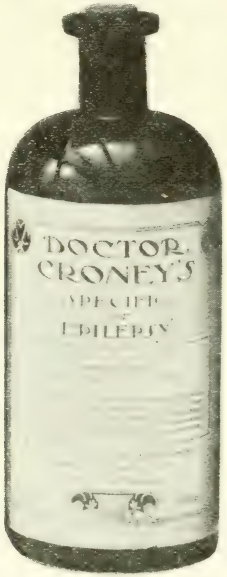
"Shorn of its mystery and secrecy," says THE JOURNAL, "Croney's 'cure' for epilepsy, like every other nostrum of its type, stands nakedly exposed as essentially a mixture of bromids."

9. THE JOURNAL A. M. A., April 17, 1915, p. 1334.

Details of Analysis

Alcohol.—The specific gravity of the 100 c.c. distillate was 0.99724 at 15.6°C. The alcohol was distilled from 50 c.c. of the original. The alcohol by volume was equivalent to 3.70 per cent.

Ammonia.—(*a*) Twenty c.c. of the original, after the ammonia distillate treatment, neutralized 6.36 c.c. of normal hydrochloric acid. This is equivalent to 0.54 gm. ammonia in 100 c.c. or 0.47 per cent. (*b*) Twenty-five c.c. of the original,



Dr. Croney's so-called "Specific for Epilepsy."

after the ammonia distillation treatment, neutralized 6.20 c.c. of normal hydrochloric acid. This is equivalent to 0.53 gm. ammonia in 100 c.c., or 0.46 per cent.

Sodium and Potassium.—Twenty-five c.c. of the solution (25 c.c. to 250 c.c.) yielded 0.3262 gm. of combined sulphate and 0.3609 gm. platinum. This is equivalent to 5.78 gm. potassium and 0.052 gm. sodium in 100 c.c., or 5.06 per cent. potassium and 0.04 per cent. sodium.

Bromid and Chlorid.—(*a*) Twenty-five c.c. of the solution (25 c.c. of 250 c.c.) was treated with 25 c.c. of 1.001 times fifth-normal silver nitrate. The weight of the combined (w)

silver bromid and silver chlorid was 0.7518 gm. and the weight of silver chlorid (a) due to excess of silver nitrate was 0.1396 gm. This is equivalent to 12.47 gm. bromin and 0.18 gm. chlorin in 100 c.c., or 10.93 per cent. bromin and 0.15 per cent. chlorin. (*b*) Treated as above, the weight of the combined (w) silver bromid and silver chlorid was 0.7516 gm. and the weight of the silver chlorid (a), due to the excess of silver nitrate, was 0.1397 gm. This is equivalent to 12.42 gm. bromin and 0.20 gm. chlorin in 100 c.c., or 10.89 per cent. bromin and 0.17 per cent. chlorin. (*c*) Method B (The weight of the combined silver bromid and silver chlorid was taken as the average of the above). The weight of silver iodid was 0.9345 gm. This is equivalent to 11.09 per cent. bromin and 0.02 per cent. chlorin. (*d*) The weight of silver iodid was 0.9488 gm. This is equivalent to 10.77 per cent. bromin and 0.24 per cent. chlorin.

Carbonate.—The carbonate was determined by using the Knorr apparatus. (*a*) Twenty c.c. of the original yielded 0.1664 gm. of carbon dioxid. This is equivalent to 1.13 gm. carbonate (CO_3) in 100 c.c., or 0.98 per cent. carbonate (CO_3). (*b*) Twenty c.c. of the original yielded 0.1671 gm. carbon dioxid. This is equivalent to 1.13 gm. of carbonate (CO_3) in 100 c.c., or 0.99 per cent. carbonate (CO_3).

PART II

REPORTS ABSTRACTED AND REPRINTED FROM THE JOURNAL A. M. A. AND FROM THE REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY

DEAD SHOT COUGH REMEDY

(Reprinted, with additions, from The Journal A. M. A., April 17, 1915, p. 1348)

The laboratory examines preparations which are sold locally only when because of special features they are of general interest to the profession. In such cases the examination is carried only far enough to bring out the points of special interest. A case of this kind is a preparation called "Dead Shot Cough Remedy," which, because of its dangerous nature, seemed to call for an exposé. The following inquiry was received by THE JOURNAL:

"*To the Editor:*—I am sending you a one-half ounce vial of Dead Shot Cough Remedy in original package. The person who puts up and peddles this claimed that it contained no alcohol, opium or any harmful drug, and was a sure cure, etc. A party took two doses and complained of suffocation and an enlargement of the blood vessels of the head, blindness, vertigo and afterward a violent headache. Also, another party took 10 drops and complained of a fulness in head and dyspnea—says it feels as if all the blood goes to the head. It seems to have the effects of the nitrites. The label does not declare its contents and the preparation is put up and sold by a layman. Can you examine and report the findings of the contents of this bottle, and whether this is being put up and sold in violation of the Pure Food and Drugs Act?

R. L. ALEXANDER, M.D.; Jayton, Texas."

The specimen sent in had an overpowering odor reminding one of fusel oil. In view of its evident potency and the consequent danger liable to result from its promiscuous use,

the Chemical Laboratory of the Association was asked to make an examination of the specimen. The following is the report:

The specimen submitted to the laboratory for examination was labeled:

DEAD SHOT COUGH REMEDY

Dead shot for coughs, and colds. Manufactured and sold exclusively by W. F. Martin, Anson, Texas. Dose: From 12 to 15 drops for aoults three or four times a day without water. Give children number of drops, according to age.

Tests were made for the presence of such compounds as amyl nitrite and nitroglycerin, either of which might produce the symptoms reported by those using the preparation, but the presence of neither compound could be demonstrated. On evaporating some of the preparation, a small amount of an oily residue was left which from its physical properties was concluded to be kerosene, or a similar petroleum oil.

Compared with a known specimen of amyl acetate as to odor, color, taste, volatility, presence of acetate and reaction with vanillin sulphuric acid reagent, no difference could be detected.

This qualitative examination indicates that the specimen of liquid sent to the laboratory is essentially amyl acetate containing a small amount of kerosene or similar oil.

As to physiologic effects of amyl acetate, Koelsch (*Hyg. Rundschau*, 1913, p. 239) states that it produces coughing, dizziness and severe headache. Fraenkel ("Arzneimittel Synthese," Edition 3, p. 70) states that amyl acetate is very energetic and quick acting, affecting the respiration very markedly and in larger doses having a paralyzing effect on the nerve centers.

These statements show that amyl acetate is an active compound, and some of the symptoms ascribed to it are the same as those reported by Dr. Alexander's patients.

THE JOURNAL commented as follows:

"The Food and Drugs Act, commonly called the 'Pure Food and Drugs Act,' is a federal law and affects only products which are sold in interstate commerce. As the preparation is said to be sold locally only, the federal law does not apply."

VENARSEN

(Abstracted, with additions, from The Journal A. M. A., May 22, 1915, p. 1780)

Venarsen is prepared by the Intravenous Products Company, Denver. The advertising circulars contain inconsistent statements as to its composition. According to one circular Venarsen is

". . . a comparatively non-toxic organic arsenic compound, 0.6 Gm. representing 247 Mg. (3¾ grains) of metallic arsenic in chemical combination. . . ."

According to another circular Venarsen is

". . . a comparatively non-toxic organic arsenic compound, 0.6 Gm., representing 247 Mg. (3¾ grains) of metallic arsenic and .78 Mg. (1/250 grains) metallic mercury in chemical combination."

Neither one of these statements gives any information as to the actual composition of the product. The Council on Pharmacy and Chemistry addressed to the manufacturers an inquiry which elicited the reply that:

"Venarsen contains in each 5 c.c. 0.6 Gm. Sodium Dimethyl Arsenate, .0016 grams of Mercuric Iodide, .0048 grams of Sodium Iodide in solution in a suitable vehicle for intravenous administration."

At the request of the Council the Association's Chemical Laboratory examined Venarsen and reported:

Three ampules of Venarsen were examined. The first ampule was labeled

"A comparatively non-toxic organic arsenic compound, representing 247 Mg. (3¾ grs.) of metallic arsenic in chemical combination. 5 c.c. — 0.6 Gm."

Practically the same statement appeared in an advertising circular wrapped around the ampule. The second and third ampules bore labels identical with the first. The circulars differed from that accompanying the first ampule in that the presence of mercury is also announced, thus:

"Venarsen is a comparatively non-toxic organic arsenic compound, 0.6 Gm., representing 247 Mg. (3¾ grains) of metallic arsenic and .78 Mg. (1/250 grain) metallic mercury in chemical combination and is so prepared and enhanced as to present the ingredients to the blood in their most acceptable form."

Thus, although the potent elements said to be contained in Venarsen are named, its chemical character (the combination in which the elements occur) is not disclosed.

The ampules contained a transparent, odorless solution, possessing the yellow color of salvarsan solution (an aqueous solution of sodium cacodylate, mercuric iodid and sodium

iodid in the amounts said to be present in Venarsen is colorless). Qualitative tests demonstrated the presence in each of the three ampules of sodium cacodylate (sodium dimethyl arsenate), and the absence of arsenites, arsenates, phosphates, arsanilates (atoxyl, soamin) and arsenphenolamins (salvarsan, neosalvarsan). Titrated with normal hydrochloric acid, using methyl orange as indicator (as outlined in New and Nonofficial Remedies, 1915, p. 40), the three ampules were found to contain the equivalent of respectively, 0.219, 0.253 and 0.216 gm., or an average of 0.244 gm. arsenic. (According to statements of the firm each 5 c.c. of Venarsen contains 0.6 gm. sodium dimethyl arsenate (sodium cacodylate), equivalent to 0.247 gm. arsenic or 41.66 per cent. Sodium dimethyl arsenate, as described in New and Nonofficial Remedies, contains 3 molecules of water and 35 per cent. arsenic. This indicates that the sodium dimethyl arsenate used in Venarsen contains less water of crystallization than the N. N. R. product).

Neither mercury nor iodid could be found in the first ampule. (The company has since explained that mercury was absent only from the first experimental samples). The second and third ampules contained iodid and mercury in small amount. The exact quantity was not determined because, on the basis of the mercury content declared, a single accurate mercury estimation would have required the purchase of something like 25 to 100 ampules. As each ampule sells for two dollars, the cost of the material was considered prohibitive.

From the foregoing we conclude that the first ampule examined consisted essentially of a solution containing 0.625 gm. of sodium cacodylate, N. N. R., while the second and third ampules contained 0.722 gm. and 0.617 gm. sodium cacodylate, respectively, and in addition, a mercury compound, probably mercuric iodid, dissolved by sodium iodid.

The Council, in its report, commented on the laboratory findings as follows:

"In other terms, Venarsen as now marketed is a simple solution containing approximately 9 grains of sodium cacodylate, 1/40 grain of mercury "biniodide" and $\frac{3}{4}$ grain of sodium iodid to each full dose. . . . Venarsen treatment consists essentially in the intravenous injection of large doses of sodium cacodylate. The other ingredients, as well as the name, merely constitute so much mystification.

Details of Analysis

Before examining Venarsen, sodium cacodylate and a solution containing sodium cacodylate, mercuric and sodium iodid were examined.

A market specimen of sodium cacodylate was assayed by titration as outlined in New and Nonofficial Remedies, 1915, p. 50. Thus 0.9864 gm. sodium cacodylate dissolved in 20 c.c. water, and methyl orange added, required 4.78 c.c. normal acid for neutralization, equivalent to 75.77 per cent. anhydrous sodium cacodylate; and 1.7828 gm. required 8.44 c.c. normal acid, equivalent to 75.71 per cent. anhydrous sodium cacodylate, an average of 75.74 per cent.

A solution was then made containing in 100 c.c. sodium cacodylate 12 gm., mercuric iodid 0.032 gm. and sodium iodid 0.096 gm. Of this solution 10 c.c. samples were taken and titrated as above. (*a*) one sample required 5.67 c.c. normal acid; and (*b*) another required 5.65 c.c., an average of 5.66 c.c., which calculated to the anhydrous salt indicates that the sodium cacodylate used was 75.54 per cent. anhydrous. This agrees with the titration of the sodium cacodylate alone and shows that this method of determination of sodium cacodylate is applicable in this mixture.

The examination of the Venarsen ampules was then taken up. The solution in the ampules was found to be a clear, light yellow liquid, without odor and having an alkaline reaction toward methyl orange. In each case the ampule was opened and thoroughly washed out to a beaker, methyl orange added and titrated with normal hydrochloric acid. One ampule (A) required 2.89 c.c. normal acid, equivalent to 0.219 gm. arsenic in the form of sodium cacodylate; a second ampule (B) required 3.38 c.c. acid equivalent to 0.253 gm. arsenic and a third ampule (C) required 2.93 c.c. acid, representing 0.216 gm. arsenic; an average of 0.244 gm. arsenic, agreeing with the claimed arsenic content, 0.247 gm.

Since the ampules were claimed to contain 0.6 gm. of sodium cacodylate, representing 0.247 gm. arsenic, the brand of cacodylate used must have had less water of crystallization than the kind described in N. N. R., for 0.6 gm. sodium cacodylate N. N. R. contains 0.215 gm. arsenic.

As a check on the cacodylate titration, phenolphthalein was added at the end of each titration and titrated with alkali. As the acid titration converted the sodium salt to the free acid, which is monobasic to phenolphthalein, the back titration with normal alkali should equal the acid titration, if no other substance reacting alkaline or acid were present. Ampule A required in back titrating 2.89 c.c.; Ampule B required 3.40 c.c.; and C required 2.93 c.c., all agreeing with the respective acid titrations.

As phosphates titrate in a similar manner, qualitative tests were made for their presence, but none could be detected with either magnesium mixture or molybdate solution.

To test for the presence of cacodylate some of the Venarsen was treated with hypophosphorous acid and allowed to stand. After a time the characteristic and disagreeable odor

of cacodyl was apparent. This test is not given by disodium monomethyl arsenate, nor by such arsenic compounds as salvarsan, atoxyl, soamin, etc. The flame test showed decided evidence of the presence of sodium. Venarsen does not respond to the tests of identity for salvarsan as given in N. N. R. or for neosalvarsan, atoxyl, soamin or arsacetin. Therefore it was concluded that sodium cacodylate was the only organic arsenic present.

Venarsen from Ampule A when treated with ferric chlorid and hydrochloric acid and shaken with chloroform yielded no color to the chloroform, indicating the absence of iodids. When made acid by hydrochloric acid and boiled with copper foil and the latter then heated in a small tube, no mercury could be detected. In the other two ampules both mercury and iodid were found by these tests. From these tests it was concluded that the first ampule contained only sodium cacodylate and the other two a mercury compound and an iodid, confirming qualitatively the claims of the manufacturers. No quantitative determinations of mercury or iodid were made, as from 25 to 100 ampules would be necessary to make an accurate determination.

TANLAC

(Abstracted, with additions, from The Journal A. M. A., June 5, 1915, p. 1930)

Tanlac is a product of the Cooper Medicine Company, Dayton, Ohio. It contains 17 per cent. alcohol and is a "tonic and system purifier." The claims made for Tanlac are of the usual extravagant type.

"Tanlac . . . is not what is commonly called a medicine; it is more than a medicine, being the liquid maximum strength of medicinal properties of a plant discovered by Cooper's uncle, a celebrated scientist, which plant properties, together with other ingredients, obtained their high efficiency under the personal direction of Herr Jos. Von Trimbach, a native German chemist of note in charge of the Cooper laboratory."

"Tanlac is called the magic medicine . . ."

"Tanlac . . . preserves your health, gives you renewed energy, brightens your spirits, lengthens your life . . ."

A number of inquiries having been received regarding this nostrum, a study of its composition was thought to be of interest.

One original bottle of Tanlac was submitted to the Chemical Laboratory for examination. The bottle contained 8 ounces of a brown liquid, having a wine-like odor, and also an odor somewhat resembling wild cherry. The taste was

very bitter, like that of gentian. The specific gravity of the liquid at 15.6 C. was 1.0205. Qualitatively, the following were detected. Alkaloids were present, out of which berberin was isolated and identified. Hydrastin and the commoner alkaloids were not found. Other alkaloids besides berberin were present, but not identified. Tests for emodin was positive. Acid caused precipitation; this precipitate had an odor of licorice. After purification, and treatment with ammonia, the ammonium salt of glycyrrhizic acid was detected. A relatively large proportion of glycerin was present. A small amount of tartaric acid was detected, which would indicate a wine. The residue, after heating on a steam bath for twelve hours, and drying over sulphuric acid for an equal time, weighed 11.1 per cent. By far the greater amount of the residue was glycerin. The ash was 0.25 per cent. The amount of alcohol was found to be 15.70 per cent. of absolute alcohol by volume. The weight of the alkaloids was 0.017 per cent.

From the examination, it is concluded that Tanlac is probably a vinous extract which contains essentially a bitter drug (such as gentian), an emodin-bearing drug (such as buckthorn, rhubarb or cascara), a berberin-bearing drug (such as berberis aquifolium), glycyrrhizic acid (from licorice), flavored with wild cherry, and to which has been added a relatively large proportion of glycerin.

Accompanying the bottle of Tanlac were some Tanlac Laxative Tablets. These contained phenolphthalein.

The comments of THE JOURNAL were as follows:

"The findings of the chemists indicate that Tanlac is essentially a wine to which have been added some bitter herbs, a small amount of laxative and some glycerin."

Details of Analysis

Berberin.—Twenty-five c.c. of the original was made ammoniacal and shaken with three separate portions of chloroform. The combined chloroform extraction, yellow in color, was evaporated to dryness and the residue taken up in acidulated water. This was treated with iodin, T.S., the precipitate filtered and washed. The alkaloidal precipitate was then treated with sodium sulphite solution, this made ammoniacal and the alkaloids extracted with chloroform as above. After evaporation of the chloroform, a few drops of dilute hydrochloric acid was added, and again the whole evaporated to dryness on the steam bath. The hydrochlorids of the alkaloids were taken up in water, and potassium iodid added. A yellow precipitate formed. After removing this precipitate, and converting to the free alkaloid, it responded to tests for berberin with nitric acid and with Froehde's reagent.

Emodin.—Acidulating some of the solution, extracting with benzol, and then shaking with ammonia water, imparted the characteristic color test to the aqueous solution.

Glycerin.—After evaporating some of the original to a syrup, the usual acrolein test affirmed the presence of glycerin.

Tartaric Acid.—About 60 c.c. of the original was used. The alcohol was removed, the whole diluted, and an excess of lead acetate added and the precipitate removed by filtration, and washed well. The precipitate was then transferred to about 170 c.c. of water and the lead salts decomposed by hydrogen sulphid. After removal of the lead sulphid, the filtrate was evaporated to a small volume, filtered, and this filtrate tested for tartaric acid. A one-half portion was treated with one or two drops of ferrous sulphate solution, one or two drops of hydrogen peroxid added, and then a slight excess of sodium hydroxid. This gave a blue color, which, however, was soon masked by the intense red of acetate of iron.

Wild Cherry.—The odor caused wild cherry to be suspected. During various operations the odor of hydrocyanic acid was somewhat discernible. Test for hydrogen cyanid was faintly positive. It was concluded that wild cherry was probably present.

Alcohol.—Fifty c.c. of the original was delivered into a distillation flask, and the alcohol determination made as described in the Provisional Methods of the Association of Official and Agricultural Chemists, Bulletin 107, p. 83. The specific gravity of the hundred c.c. distillate was 0.98893. This is equivalent to 15.70 per cent.

HERBETTA CURINE

(Reprinted from The Journal A. M. A., June 12, 1915, p. 2006)

Herbetta Curine is put on the market by the Herbetta Medicine Co., Indianapolis, Ind. According to the advertising matter:

"Herbetta Curine is not an old remedy worked over . . . it is not a nostrum or patent medicine. It is a scientific combination of four tablets discovered only after prolonged and diligent experience and research."

The company says that Herbetta Curine is not a cure-all; it is merely intended:

"To improve the digestion and assimilation of food."

"To restore tone and vigor to the wornout and exhausted nervous system."
"To restore the natural action of the liver, kidneys and bowels."
"To make rich blood."
"To put health and life into the whole body."
"To restore the sexual organs to their natural functions."

A specimen of Herbetta Curine was received from a correspondent recently. The package contained three envelopes labeled 1, 2 and 3, respectively, and in addition a number of red tablets. The following examination is reported by the Association's laboratory:

ENVELOPE No. 1:—This contained small, light green tablets. Tests indicated that these tablets contained a water-soluble phosphate of iron.

ENVELOPE No. 2:—This contained small gray tablets which were very bitter and probably consisted essentially, or largely, of some "bitter tonic."

ENVELOPE No. 3:—This contained small green tablets which responded to tests for aloes and aloin. These tablets constituted the laxative agent in the "treatment."

RED TABLETS:—These had a strong odor of sassafras and tests indicated that they were essentially strontium and potassium bromid.

Each "treatment" costs $5 and the company offers to issue a "guarantee" to the effect that after thirteen treatments are taken the victim may have subsequent treatments for $1.50 each "as long as treatment may be needed."

LEPSO

(Abstracted from The Journal A. M. A., June 12, 1915, p. 2006)

Lepso, a preparation advertised as an epilepsy cure, is sometimes advertised under the name of M. Lepso, Box 226, Milwaukee, Wis., and at other times by the Lepso Company, Island Avenue, Milwaukee. After an analysis of Lepso the Laboratory reported:

From the weight of the silver halid precipitate, it is calculated that Lepso contains bromids equivalent to about 22.5 gm. in 100 c.c.

As the dose recommended was one half ounce, this was equivalent to giving 3.4 gm. (51 grains) of potassium bromid to the dose. Such a mixture is dangerous, yet it may be sold indiscriminately to the public without warning or even mention of presence of bromids.

IODEX

(Reprinted, with additions, from The Journal A. M. A., June 19, 1915, p. 2085)

Iodex is manufactured by Menley and James, Ltd., New York. It is advertised as

". . . an embodiment of vaporized iodin in an organic base, reduced and standardized at 5 per cent. by incorporation with a refined petroleum product."

The advertising conveys the impression that the effects of free iodin are to be obtained from the preparation; it is said to contain "5 per cent. Therapeutically Free Iodine," and to do

". . . everything the doctor expects of FREE iodin employed by inunction, without one physical or therapeutic drawback."

The statements are also made that the preparation "neither stains, irritates, blisters or cracks the skin, and that "thirty minutes after inunction iodin can be found in the urine."

The following report of an examination made by the Chemical Laboratory of the American Medical Association has been submitted to the Council:

Iodex is dark green, practically black, with a slight odor of oleic acid. The green color is apparent when the ointment is rubbed on the skin, but disappears on continued rubbing. This nonstaining property is explained by the results of a test for free iodin, made on five specimens, four of which yielded only minute traces of free iodin, while the fifth yielded none. Of course, the statements that Iodex is an "Effective Free Iodin Application Without Drawbacks" and also a means of "Really Efficient External Iodine Therapy Without Stain or Irritation" contradict each other. Free iodin cannot be present in a sufficient quantity to be therapeutically efficient in any application which does not stain the skin.

The total iodin content of the five specimens was found to be 2.63 per cent.—a little over one half of the content claimed.

Absorption and excretion experiments were performed to test the claim that "thirty minutes after inunction iodin can be found in the urine." In several subjects, from 1 to 2 gm. of Iodex was rubbed on the skin of the forearms, and the urine, for periods varying from seven to seventy-two hours, was collected and tested for iodin. In all of the tests the results were negative.

THE JOURNAL, in conclusion, observed:

"Iodex is advertised as beneficial in muscular soreness, sprains, sciatica, neuritis, chronic rheumatism, enlarged glands, orchitis, epididymitis, gout, burns and dermatomyco-

ses. It is also said to be 'Indicated in Glandular Enlargements, Inflammatory Conditions, Various Joint Diseases, Rheumatism, Skin Diseases, Chilblains, etc., etc.'

"To sum up:

"1. As shown in the foregoing laboratory report, the composition is incorrectly stated, for the actual iodin content is only about half of that claimed.

"2. It is not true that the action of Iodex is essentially that of free iodin, which is the impression conveyed by the advertising.

"3. The assertion made in the advertising, that iodin may be found in the urine shortly after Iodex has been rubbed on the skin, has been experimentally disproved.

"In view of these findings, the Council voted that Iodex be refused recognition for conflict with Rules 1, 4 and 6."

Details of Analysis

Iodex is completely soluble in chloroform, but only partially soluble in alcohol, and insoluble in water. Saponification with an alcoholic solution of potassium hydroxid leaves an unsaponified portion which has the properties of petrolatum.

As in the claim for the product, much is made of the alleged presence of free iodin, the latter was tested for. About 2 gm. of various samples of Iodex was thoroughly mixed with sand and the mixture triturated with potassium iodid, and the potassium iodid extract then tested with starch. One specimen yielded no trace of iodin and four other specimens yielded minute traces only. This, then, accounts for the nonstaining property of the preparation and proves false the claims for the presence of free iodin.

The five samples were taken, thoroughly mixed, and the total iodin determined by Hunter's method for iodin in organic compounds, after first boiling with alcoholic potassium hydroxid solution. 3.1000 gm. Iodex required 6.30 c.c. tenth-normal thiosulphate, equivalent to 0.079 gm. iodin or 2.56 per cent., 3.1280 gm. Iodex required 6.70 c.c. tenth-normal thiosulphate, equivalent to 0.0844 gm., or 2.70 per cent. iodin, an average of 2.63 per cent., or just about one half the claimed content.

Excretion experiments were made by rubbing into the skin of the forearms about 1 gm. of Iodex and collecting the urine for seven or eight hours. Each portion of urine was tested for the presence of iodid; then the whole day's output was concentrated and treated by Hunter's method for total iodin. Three persons carried out the experiment qualitatively with negative results. Then one experiment was made in which

a known quantity of iodin, viz., 1.8748 gm., was used. The urine collected subsequently during the day showed no trace of iodid. These tests show that the statements regarding the absorption and excretion of Iodex are untrue.

From the foregoing it is concluded that Iodex does not contain free iodin; that its iodin content is only about half that claimed; and that its iodin can not be detected in the urine after the use of Iodex.

While the advertisements warn against the use of imitations the British Codex gives a formula for preparing a similar ointment, "Unguentum Iodi Denigrescens B.P.C." Following the directions (viz. heat 95 gm. soft paraffin till liquid and add 5 gm. powdered iodin and heat till combination is complete), a preparation was obtained which had in general the properties of Iodex. But by following the formula of Martindale (The Extra Pharmacopoeia Edit. 14, p. 410) for "Unguentum Iodi Intinctum" a preparation is obtained which very closely simulates Iodex. This is made by heating together iodin 1 part, oleic acid 4 parts, soft paraffin 14 parts, and hard paraffin 1 part.

ANTOX

(Abstracted, with additions, from The Journal A. M. A., July 3, 1915, p. 45)

Antox is put on the market by "Dr." W. J. Garbutt of Milwaukee. Garbutt seems to put his nostrum on the market in various ways. One of these methods is by traveling over the state with a concern calling itself the "Quaker Doctors," a medicine-vaudeville show. A letter received by THE JOURNAL from a small town in northern Wisconsin described the methods of this concern, and told how the life of the writer's child had been sacrificed because it was given Antox until its condition was beyond medical help.

Original bottles of "Dr. Garbutt's Antox No. 1," prepared by Dr. W. J. Garbutt, Milwaukee, Wis., were submitted to the Chemical Laboratory for examination. Each bottle contained about 120 c.c. of a red syrupy liquid, having a sharp odor and an acid reaction. The specific gravity of the liquid at 15.6 C. was 1.0603. Qualitative tests demonstrated the presence of ammonium, chlorid, sulphite (sulphur dioxid), sulphate and invert sugar. Quantitative examination yielded the following:

Ammonia (NH_3)	0.279 per cent.
Chlorid (Cl)	0.694 per cent.
Sulphur dioxid (SO_2)	0.263 per cent.
Sulphur trioxid (SO_3)	0.018 per cent.
Invert sugar	17.47 per cent.

From these results it was concluded that essentially each 100 c.c. of the solution contains approximately 0.92 gm. of ammonium chlorid, 0.12 gm. of hydrogen chlorid (equivalent to 1.2 c.c. of diluted hydrochloric acid, U. S. P.), 0.35 gm. hydrogen sulphite (equivalent to 6 c.c. of sulphurous acid, U. S. P.), and 18.5 gm. of invert sugar. The sulphuric acid present is probably due to the oxidation of some of the sulphurous acid, and the invert sugar to the influence of acid on the original "cane" sugar. The amount of sulphur dioxid (sulphurous acid) is variable in different bottles, as was attested by determinations on the different specimens.

At about the same time the Laboratory was investigating this preparation the chemists of the Health Department of the City of Milwaukee also analyzed it. The analytical data they obtained were sent by Dr. George C. Ruhland, Commissioner of Health of the City of Milwaukee, and confirmed essentially the findings of the Association's chemists. THE JOURNAL said, in concluding:

"In brief it may be said that Dr. Garbutt's 'gift to humanity' is practically a mixture of sulphurous and dilute hydrochloric acid with small quantities of ammonium chlorid in water sweetened with syrup. The preparation is worthless."

Details of Analysis

Ammonia.—Ten c.c. of the original was placed in a Kjeldahl distilling apparatus, a pinch of finely granulated zinc, water, and sodium hydroxid added, and the ammonia thus liberated was distilled over into 25 c.c. of standard acid. The amount of acid not neutralized by the ammonia was determined by titration. (*a*) Ten c.c. of the original neutralized 1.73 c.c. of normal hydrochloric acid. This is equivalent to 0.294 gm. ammonia in 100 c.c. (*b*) Ten c.c. of the original neutralized 1.76 c.c. of normal hydrochloric acid. This is equivalent to 0.299 gm. ammonia in 100 c.c., and an average of 0.27 per cent.

Chlorid (Cl^-).—(a) Ten c.c. of the original was diluted to suitable volume, treated with an excess of silver nitrate in the presence of nitric acid, and the chlorid weighed as silver chlorid (AgCl). The amount of silver chlorid was 0.2978 gm., equivalent to 0.693 per cent. (*b*) Ten c.c., treated as above, yielded 0.2988 gm. silver chlorid equivalent to 0.695 per cent. chlorid (Cl^-).

Sulphur Dioxid (SO_2) Sulphurous Acid.—A measured amount of solution from a full bottle (which had previously been mixed with the contents of four others, and quickly refilled) was delivered into about 100 c.c. of water in an

Erlenmeyer flask, starch solution added, and then titrated with standard iodin solution. (*a*) Ten c.c. of the original required 8.40 c.c. of 1.018 times tenth-normal iodin. This is equivalent to 0.253 per cent. (*b*) Ten c.c. of the original required 8.30 c.c. of 1.018 times tenth-normal iodin. This is equivalent to 0.273 per cent. sulphur dioxid.

Sulphur Trioxid (SO_3) Sulphuric Acid.—(*a*) Twenty-five c.c. of the original was diluted with water, boiled in an Erlenmeyer flask for fifteen minutes, and an excess of hot barium chlorid solution added. The barium sulphate was filtered, ignited and weighed 0.0156 gm. This is equivalent to 0.020 per cent. sulphur trioxid. (*b*) Twenty-five c.c. of the original, treated as above, yielded 0.0126 gm. barium sulphate. This is equivalent to 0.016 per cent. sulphur trioxid.

Sugar.—Twenty-five c.c. of the original was made up to 500 c.c. with water, an aliquot portion of this was treated with Fehling's solution according to Allihn's method (Leach-Winton, page 608, ed. 3). The copper was precipitated electrolytically in a platinum dish, allowing a current of 0.25 amperes and 2.6 volts to pass through the solution over night. (*a*) Ten c.c. yielded 0.1769 gm. of copper, equivalent (by tables) to 17.36 per cent. sugar. (*b*) Twenty-five c.c. yielded 0.4453 gm. copper, equivalent to 17.58 per cent. sugar.

OIL-OF-SALT

(Abstracted from The Journal A. M. A., Aug. 14, 1915, p. 640)

C. A. Mosso, 2253 Warren Avenue, Chicago, exploits a nostrum "Oil-of-Salt," claimed to be "a product of salt and oils" and an "infallible destroyer of all systemic poisons."

Mosso's philosophy of health and disease is a simple one: All diseases are but "systemic poisons" in the body: Oil-of-Salt destroys all poisons; ergo, Oil-of-Salt cures all diseases.

"All of our ailments are caused from some poison contracted in devious ways. . . ."

Mosso's Oil-of-Salt will remove any and all kinds of systemic poison from the human body . . . and when this is done perfect health is the natural result."

"Mosso's Oil-of-Salt is proclaimed to be the most wonderful curative agency known. . . ."

The favorite method of introducing this preparation seems to be that of sending to those in charge of manufacturing plants, a printed letter reading, in part, as follows:

"*Gentlemen:*—If you will allow me to place in the hands of your First Aid Department my system in the line of a First Aid to the Injured, I will guarantee that no workman need lay idle for over thirty minutes, after the treatment has been applied, from any of the ordinary accidents that occur in their daily work, also that they will not suffer from any pain after said time, and there will never be any bad effects from the wounds.

"The wounds I speak of are as follows: Cuts, Burns, Strains, Crushed Feet and Hands, also all Poisonous Wounds as those caused from Rusty Nails, Copper, Brass, Lead, Zinc, etc. No Blood Poison can ever take place in any case where The First Aid is used.

"You need have no fear of death from the following troubles, and relief can be obtained in from thirty to sixty minutes, namely; Ptomaine Poisoning, Internal Hemorrhage of any kind, Colic, Bloody Disentary [*sic*] and all dangerous afflictions that assail mankind in their daily life."

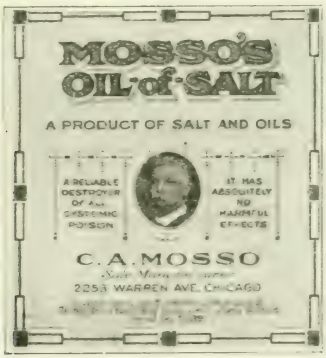
One would imagine that it would not take medical knowledge to recognize the absurdity of the claims made in this letter. Several manufacturing concerns, however, have written to THE JOURNAL asking for information regarding the composition and probable value of Mosso's Oil-of-salt and, as a result, an analysis was made of the preparation. The chemists' report from the laboratory of the American Medical Association follows:

Mosso's Oil-of-Salt is a yellow oily mixture possessing an aromatic odor, resembling a mixture of turpentine, camphor and sassafras, and possessing a strong burning taste. It is inflammable, and burns with a luminous smoky flame.

When distilled with steam it leaves a yellow oily liquid devoid of aromatic odor, but possessing an odor and taste indicating linseed oil. Qualitative tests and the iodin absorption number further identify the oil as linseed oil. The volatile portion which was carried over by the steam was a colorless oily mixture and possessed the same characteristic odor as Oil-of-Salt. This mixture was completely volatile on the steam bath and was inflammable.

Quantitatively the linseed oil was determined by removing the volatile constituents by steam, and extracting the linseed oil by chloroform and evaporating the chloroformic solution in a weighed dish. After evaporation of the chloroform the oil was allowed to dry in a desiccator. After a short time the weight began to increase, this no doubt being due to oxidation. The weight of oil found by this method may be taken as a close approximation of the actual content of oil; the presence of about 63 per cent. linseed oil was indicated. By heating a weighed sample of Oil-of-Salt on a boiling water-bath until the characteristic aromatic odor of the preparation had disappeared a residue amounting to 64.5 per cent. was left. This approximate determination indicates the non-volatile oil (linseed) content to be about 63 to 64 per cent.

An aqueous extract of Oil-of-Salt is acid in reaction to litmus, methyl orange, phenolphthalein and dimethylamino-azobenzene and contains chlorid, showing the presence of free hydrochloric acid. A portion was extracted with water until the extracts no longer were acid to methyl orange and the combined extract titrated with normal alkali. This showed the presence of 0.16 per cent. free hydrochloric acid. After titration the solution was made acid by nitric acid and the chlorid precipitated as silver chlorid. By this method a chlorid content equivalent to 0.17 per cent. hydrochloric acid was indicated. An alcoholic solution of Oil-of-Salt titrated with normal alkali in the presence of phenolphthalein indicator showed the presence of 0.17 per cent. free hydrochloric acid.



Photographic reproductions of the labels of "Mosso's Oil-of-Salt" and of "First-Aid Treatment" which is said to be the later name of the Mosso preparation.

These determinations agree as to the free hydrochloric acid content. A total chlorid determination made after fusing with Hunter's fusion mixture showed a chlorid content of 0.51 per cent. equivalent to 0.52 per cent. hydrochloric acid. An alcoholic extract of Oil-of-Salt, made until evaporation of some of the alcohol showed no more of the volatile oils, was fused with Hunter's mixture and the chlorid determined; 0.489 chlorid equivalent to 0.49 per cent. hydrochloric acid was found. This compared with the total chlorid content indicates that the part of the mixture containing the chlorid is soluble in alcohol, viz., the volatile oils.

In general it may be concluded that Oil-of-Salt is a mixture consisting of about two thirds linseed oil with one third of a mixture of essentials oils including turpentine, camphor

and sassafras, containing total chlorids equivalent to 0.52 per cent. hydrochloric acid, one third of which is present as free hydrochloric acid.

THE JOURNAL commented on this report as follows:

"Here, again, we have illustrated the reason for the frantic opposition on the part of "patent medicine" manufacturers to every demand for publicity of composition. The most ignorant of workmen could hardly be fooled into believing that a mixture of linseed oil with small amounts of oils of turpentine, camphor and sassafras, a pinch of salt and a trace of muriatic acid could produce the results that Mosso claims for his 'Oil-of-Salt.' With the mystery that surrounds a secret mixture like Oil-of-Salt, however, any claim, no matter how preposterous, will be accepted by a certain number of people.

"The latest information regarding Oil-of-Salt indicates that it is being exploited under the name, 'First Aid Treatment,' and sold by the Pan-Alert Laboratories, 607 Marquette Building, Chicago."

URICSOL

(Abstracted, with additions, from The Journal A. M. A., Aug. 14, 1915, p. 638)

At the request of the Council on Pharmacy and Chemistry the Association laboratory took up the chemical examination of Uricsol, which is marketed by the Uricsol Chemical Company, formerly of Los Angeles, now of Boston. Regarding its composition only vague statements are made. In an advertising pamphlet it is promised that the formula will be sent to physicians on request. Such a request from a physician elicited the following statement:

"Uricsol is a non-irritating, alkaline solution, containing Lithium Citrate, Acid Citric and Potassium Nitrate, together with a saline laxative in the form of Glycero Sodium Phosphate, with vegetable Tonics added."

With this meager information as a basis the examination was taken up. A trade package purchased in March, 1915, from a wholesale drug house was labeled:

"Uricsol Rheumatic Remedy, Uric Acid Solvent, Kidney and Liver Stimulant, Manufactured by the Uricsol Chemical Co., Los Angeles, Cal."

This package was wrapped in a circular entitled "The Great California Remedy—Uricsol." The preparation is a viscid, slightly turbid light brown liquid, with a faintly aromatic odor and a salty, bitter taste. The diluted solution is acid in reaction toward litmus and phenolphthalein and alkaline toward methyl orange.

Qualitative tests showed the presence of phosphate, citrate, nitrate, sodium, glycerin, and a small amount of lithium in aqueous solution. Besides these a small amount of some organic, nonalkaloidal substance was found, which from its bitter taste suggested gentian. From the qualitative tests it appeared that the phosphate was the predominating ingredient and accordingly a phosphate determination was made. The phosphate was determined as magnesium pyrophosphate. Ten c.c. of Uricsol was diluted to 250 c.c. and 20 c.c. aliquots taken. The first aliquot yielded 0.1600 gm. magnesium pyrophosphate and the second yielded 0.1557 gm., an average of 0.1598 gm. This is equivalent to 64.20 gm. sodium phosphate U.S.P. per 100 c.c. of Uricsol. This amount of sodium phosphate is made possible by the presence of the citric acid and sodium nitrate present.

Uricsol evidently is a solution containing a large amount of sodium phosphate with small amounts of lithium, nitrate, citric acid and glycerin with probably some vegetable extract.

In general Uricsol is similar to the once widely exploited proprietary "Melachol," which has been frequently imitated. A preparation, essentially identical, is in the United States Pharmacopeia, under the title "Compound Solution of Sodium Phosphate."

On the basis of the foregoing results the Council on Pharmacy and Chemistry concluded that "Uricsol is a mixture of well-known drugs marketed with false claims as to therapeutic action, with misleading and meaningless statements as to composition and under a name which invites uncritical prescribing. Uricsol is held ineligible to inclusion in New and Nonofficial Remedies."

Details of Analysis

The phosphate was determined as magnesium pyrophosphate. Ten c.c. Uricsol was diluted to 250 c.c. and 20 c.c. aliquots, equivalent to 0.8 c.c. of the original material. The first determination yielded 0.1600 gm., and the second, 0.1597 gm., an average of 0.1598 gm. magnesium pyrophosphate. Calculated to $Na_2HPO_4.12H_2O$, this would be equal to 0.5136 gm. or 64.20 gm. per 100 c.c. of Uricsol.

FISHER REMEDY—A MERCURY NOSTRUM

(Abstracted, with additions, from The Journal A. M. A., Aug. 21, 1915, p. 733)

A correspondent wrote to THE JOURNAL:

"Under separate cover I am sending in its original box a capsule which is reported to contain no mercury, but to be a specific cure. Five capsules sell for $25. The physician directs the patient to take courses of five capsules, one capsule each day, with an interval of three weeks between courses. The patient is warned against taking milk, oysters or liquor during the administration of the drug and for two or three days thereafter.

"This treatment was taken by a patient of ours who had multiple gummas of the ribs, which healed under its administration, leaving him, however, with an extreme thirst, extreme polyuria, loss of weight and anemia. This patient, after taking four capsules, became so nauseated that he refused to take the fifth.

Could you give me any data about the remedy, or must I conclude that these symptoms are an extension of the disease rather than the effect of the treatment?

WILLIAM N. ANDERSON, M.D., Omaha.

The letter and specimen were submitted to the Chemical Laboratory, which reports:

The small square pill box sent by Dr. Anderson, containing one capsule, bore a label with illustrations of five capsules. On the center capsule the word "Hero" appeared, and around it the inscription "Fisher Remedy. A Treatment for All Blood Diseases. Trademark registered. Manufactured by N. Bergman & Co., San Francisco, U. S. A."

The single capsule contained a grayish, moist mass weighing 1.07 gm. and possessing a slight licorice-like odor. When treated with water, the mass rapidly disintegrated; and when the mixture was poured into a tube, a heavy lemon-yellow substance settled to the bottom, followed by a layer of gray material. Some of the mixture when examined microscopically showed the presence of starch, licorice root and small globules which had the characteristic appearance of metallic mercury. Some of the gray substance when treated with dilute hydrochloric acid yielded carbon dioxid, and the solution after filtering responded to tests for calcium. Some of the gray residue on the filter when examined microscopically showed more clearly than before the presence of metallic mercury globules. A portion of this residue when gently heated in a small tube yielded a sublimate of globules

which were definitely identified as mercury. From these qualitative tests it appears that the gray part of the mixture is probably hydrargyrum cum creta, since it contains both mercury and chalk, with some starch and some powdered licorice root.

The light yellow heavy substance was separated by washing off the lighter substances with a stream of water. It was found to be a heavy lemon-colored powder, without odor and practically tasteless and soluble in hydrochloric acid. The hydrochloric acid solution thus prepared responded to test for both mercury and sulphate. As both mercurous and mercuric sulphates are white, this substance is without doubt the basic mercuric sulphate also known as "Turpeth Mineral."

As the sample of the specimen was small no attempts were made to make the determinations quantitative, but from our examination it is concluded that the capsule contains a mixture essentially of mercury with chalk and mercuric subsulphate, with some starch and licorice root as excipients.

As basic mercuric subsulphate has emetic properties it is probable that the patient's nausea, mentioned in Dr. Anderson's letter, was due directly to this drug.

This preparation is probably a new form of a mixture put out in the form of boluses a few years ago by one Fisher in Shirland, Ill. These boluses were irregular in shape and size but were practically identical in composition with the capsule just examined, as they also contained mercury with chalk, mercuric subsulphate, and an excipient.

JINTAN — A CHINESE NOSTRUM

(Abstracted from The Journal A. M. A., Aug. 28, 1915, p. 821)

A correspondent sent to the Laboratory a specimen of a Chinese preparation called Jintan, with the statement that it was very widely advertised in China. The correspondent wished to know the composition of the preparation and its approximate cost. The specimen consisted of small reddish-brown pills and was said to have been made by H. Morishita in Japan.

The pills were examined and the following report was made:

Qualitative tests indicated the absence of potent alkaloids, iron and other heavy metals, saline laxative salts and emodin-bearing cathartics such as rhubarb, aloes or cascara

in therapeutically effective amounts. Sugars were present in considerable quantities and the pills were highly aromatized, suggesting "breath perfumes" like "sen sen." A vegetable drug was present but was not identified. Physiologic experiments indicated that the pills possessed no material potency.

As the unidentified drug is likely to be of Japanese or Asiatic origin, and as the pills appeared to be devoid of therapeutically active drugs, no great amount of time was spent in an attempt to recognize this drug.

THE JOURNAL commented as follows:

"While the reported examination is not exhaustive, it seems to demonstrate sufficiently the general worthlessness of the nostrum. We cannot estimate the cost of the ingredients, but we venture a conjecture that the principal expense in the business is the advertising."

PISO'S TABLETS AND MICAJAH'S WAFERS

(Abstracted from The Journal A. M. A., Sept. 25, 1915, p. 1128)

A number of years ago Micajah's Medicated Uterine Wafers were analyzed in the Chemical Laboratory of the Association. In commenting on the laboratory's report on these wafers[1] THE JOURNAL referred to the fact "that the same interests that control Piso's Consumption Cure also control Micajah's Medicated Uterine Wafers. . . ."

According to such information as we have on file, Micajah & Co. is practically a trade name under which William A. Talbott does business; William A. Talbott is secretary and manager of the Piso Company, and he and his sister are said to control the Piso concern.

The original report on Micajah's Wafers stated that the product had, approximately, the following composition:

Alum, dried	59.86 per cent.
Borax, dried	15.62 per cent.
Boric acid	5.67 per cent.
Water of hydration	18.85 per cent.

The practical identity of the manufacturers of Piso's Tablets and Micajah's Uterine Wafters suggested the likelihood of the identity of the "tablets" and "wafers" themselves and it seemed worth while to analyze both of these products

1. This appeared in THE JOURNAL A. M. A. March 26, 1910, p. 1070; it is reprinted in the Report of the Chemical Laboratory, 1910, p. 18, and in the "Propaganda for Reform," ed. 9, p. 240.

and compare them. This was done and the report of the Association's laboratory follows:

Original specimens of "Micajah's Medicated Uterine Wafers" and "Piso's Tablets," respectively, were submitted to the Chemical Laboratory for examination. The pasteboard box, labeled "Micajah's Medicated Uterine Wafers," manufactured by Micajah & Co., Warren, Pa., contained twenty-five hexagonal wafers. Piso's Tablets, manufactured by Piso Company, Warren, Pa., consisted of 12 cylindrical tablets in a cylindrical wooden box.

Both "Micajah's Wafers" and "Piso's Tablets" are white, odorless and possess an astringent taste. They are soluble in water with difficulty, the resulting solution being acid to litmus. Hot hydrochloric acid and alkali hydroxids dissolve the powdered substances, leaving a small amount of residue. In both cases lycopodium was identified by microscopic comparisons. Both "Micajah's Medicated Uterine Wafers" and "Piso's Tablets" responded to the same qualitative tests, affirming the presence of aluminum, sodium, potassium, borate, sulphate and a trace of fatty material. From the difficulty in effecting solution, the alum in both cases is probably "burnt" alum.

Quantitative comparisons gave the following results:

	Micajah's Wafers	Piso's Tablets
Average weight	About 10.0 gr.	About 10.0 gr.
Water	19.96 per cent.	19.91 per cent.
Aluminum	5.78 per cent.	5.64 per cent.
Boric anhydrid (B_2O_3)	11.02 per cent.	11.92. per cent.

The acidity of the two samples was practically the same.

From this report it will be seen that, as might have been expected, "Micajah's Uterine Wafers"—"ethical proprietary"—are essentially identical with "Piso's Tablets"—"patent medicine."

Details of Analysis

I. MICAJAH'S MEDICATED UTERINE WAFERS

Aluminum.—*(a)* 0.9533 gm. of the dried specimen was dissolved in acidulated water, the small insoluble residue removed by filtration, and the filtrate made ammoniacal. The precipitated aluminum was filtered off and heated in a platinum crucible. The weight of aluminum oxid was 0.1502 gm., equivalent to 7.25 per cent. aluminum in the dried specimen. *(b)* 1.0522 gm. of the dried specimen yielded 0.1431 gm.,

aluminum oxid. This is equivalent to 7.21 per cent. aluminum in the dried specimen. The average, 7.23 per cent., equals 5.78 per cent. in the original undried sample.

Boric Anhydrid (B_2O_3).—Boric anhydrid was determined by distillation with methyl alcohol, from an acid mixture, as described in Leach-Winton's "Food Inspection and Analysis" ed. 3, p. 827. (*a*) 1.6271 gm. of the original specimen required 5.30 c.c. of normal sodium hydroxid, equivalent to 11.40 per cent. boric anhydrid. (*b*) 2.4396 gm. of the original specimen required 7.42 c.c. of normal sodium hydroxid, equivalent to 10.62 per cent. of boric anhydrid.

Water.—5.6332 gm. of the powdered specimen was heated for two hours in an electric oven at 140 C. The loss in weight was 0.7042 gm. This calculates to 19.96 per cent.

II. PISO'S TABLETS

Aluminum.—(*a*) 1.1226 gm. of the dried specimen was dissolved in acidulated water, the small insoluble residue removed by filtration, and the filtrate made ammoniacal. The precipitated aluminum was filtered off and heated in a platinum crucible. The weight of aluminum oxid was 0.1501 gm., equivalent to 7.09 per cent. aluminum in the dried specimen. (*b*) 1.0540 gm. of the dried specimen yielded 0.1399 gm. aluminum oxid. This is equivalent to 7.01 per cent. aluminum in the dried specimen. The average, 7.05 per cent., equals 5.64 per cent. in the original undried sample.

Boric Anhydrid (B_2O_3).—Boric anhydrid was determined by distillation with methyl alcohol, from an acid mixture, as described in Leach-Winton's "Food Inspection and Analysis," ed. 3, p. 827. (*a*) 0.9877 gm. of the original specimen required 3.33 c.c. of normal sodium hydroxid, equivalent to 11.80 per cent. boric anhydrid. (*b*) 1.3070 gm. of the original specimen required 7.42 c.c. of normal sodium hydroxid, equivalent to 12.05 per cent. boric anhydrid.

Water.—4.4155 gm. of the powdered specimen was heated for two hours in an electric oven at 140 C. The loss in weight was 0.7376 gm. This calculates to 19.91 per cent.

IODUM-MILLER

(Abstracted, with additions, from The Journal A. M. A., Oct. 2, 1915, p. 1202)

Iodum-Miller (Iodum-Miller Company, Kansas City, Mo.) is advertised to physicians under the implied claim that the preparation is new and original. It is said to be made from

"Soot Iodin." What "Soot Iodin" is, the company does not explain beyond making the statement that it is made from "Resublime" iodin and is soluble in water. According to the label:

". . . 45 drops equals 1 dr. by weight. Each drop equals the per cent. of iodin in 1 gr. potas. iodid."

Iodum-Miller, when analyzed in the Chemical Laboratory of the American Medical Association, was found to be essentially a solution of iodin and potassium iodid in glycerin. This, of course, disposes of the implied claim that it should be regarded as something new and original. It was found to contain 1.68 per cent. of free iodin and 1.80 per cent. potassium iodid. If the company's statement that 45 drops of Iodum-Miller weigh 1 dr. is correct, then it is obvious that 1 drop of the product equals the percentage, not of 1 gr. potassium iodid, as claimed, but of only $\frac{1}{20}$ gr. potassium iodid. This being the case the statement on the label is manifestly false and should constitute misbranding under the federal Food and Drugs Act.

Iodum-Miller is recommended for internal use in doses from ½ drop to 20 drops which, as the examination shows, is equivalent to from $\frac{1}{40}$ grain to 1 grain potassium iodid. Yet the use of this product is suggested in:

"Pneumonia, Tuberculosis, Pleurisy, Typhoid Fever, Syphilis, Catarrh of Mucous Surface of Alimentary Canal, Autotoxemia, Vomiting of Pregnancy, Rheumatism, Chronic Glandular and Organic Affections."

Its external or germicidal efficacy may be measured by the free-iodin content. The laboratory's analysis showed that this is less than one third of that of tincture of iodin. Nevertheless, Iodum-Miller is recommended for external application in:

"Pleurisy, Cough, Sore Throat, Pyorrhea . . . Blood Poison, Diseases of Uterus and appendages . . . Gonorrhea . . . Orchitis, Bubo, Prostatitis, Swellings, Enlarged Glands, Etc."

The therapeutic claims made for Iodum-Miller are so obviously extravagant that they need no discussion. In view of these facts the Council held Iodum-Miller ineligible for New and Nonofficial Remedies.

Details of Analysis

Iodum-Miller is a dark brown viscid liquid, possessing a faint but distinct odor of ether, and tasting of iodin. It is

miscible with water in all proportions, the aqueous dilutions possessing a strong iodin odor.

As Iodum-Miller is stated to contain free iodin, this constituent was tested for. A diluted solution of the preparation was extracted with chloroform, the chloroform thereby being colored violet. This color disappeared on shaking with thiosulphate solution; further, some of the residue left by evaporating the chloroformic solution, when heated volatilized in the form of violet vapors and resublimed in dark crystalline deposit. This deposit in turn was soluble in chloroform with a violet color and in alcohol with a brown color. These tests prove the presence of free iodin.

After the free iodin was removed by shaking with an excess of thiosulphate solution, the reaction of the solution, tested with litmus, was found to be neutral.

Evaporation of some of the preparation on a hot plate left a thick, slightly yellow liquid having the general appearance and physical properties of glycerin. This liquid responded further to glycerin tests as follows: When added to borax and then ethyl-alcohol added and the alcohol ignited it burned with a green flame; fused with potassium bisulphate, acrolein was formed.

Heating some of the preparation until the glycerin had all evaporated, left a small residue consisting of a small amount of organic matter and some solid crystalline substance. This was heated until the organic matter was decomposed. The white residue which remained responded to the flame test for potassium, and when it was treated in aqueous solution with ferric chlorid and hydrochloric acid and the mixture shaken with chloroform, iodin was found present. Iodin was further demonstrated by the fact that when concentrated sulphuric acid was added to the dry white residue iodin vapors were produced. No sodium or ammonium could be detected in the original preparation.

Qualitatively then, the preparation appeared to be a glycerin solution of iodin containing some potassium iodid.

QUANTITATIVE DETERMINATIONS

Specific Gravity.—This was taken at 25 C. and found to be 1.284. The substance was then washed from the specific gravity to a 250 c.c. volumetric flask and made up to 250 c.c. Aliquots were then taken from this for some of the determinations.

Free Iodin.—This was determined by taking 10 c.c. aliquots of the diluted solution mentioned above, and running in tenth-normal thiosulphate solution and shaking after each addition until the iodin color had disappeared. Thus (*a*) 10 c.c. required 1.72 c.c. and (*b*) required 1.70 c.c., an

average of 1.71 c.c. tenth-normal thiosulphate, representing 0.0215 gm. iodin or 1.68 per cent. by weight, or 2.15 gm. iodin per 100 c.c. of Iodum-Miller.

Total Iodin.—Total iodin was determined by fusing with Hunter's mixture and carrying out the Hunter method (*Jour. Biol. Chem.*, 1910, vii, 321). Thus (*a*) 0.7044 gm. of the preparation required 10.25 c.c. tenth-normal thiosulphate equivalent to 0.1290 gm. iodin, one sixth of which represents the iodin in the preparation, viz., 0.0215 gm. or 3.05 per cent.; (*b*) 0.5472 gm. required 8.01 c.c. tenth-normal thiosulphate equivalent to 0.1008 gm. iodin, one sixth of which, or 0.0168 gm., represents the iodin in the preparation, or 3.07 per cent., an average of 3.06 per cent. by weight. This is equivalent to 3.92 gm. iodin per 100 c.c. of Iodum-Miller.

Combined Iodin.—The difference between the free and the total iodin was taken as the amount of iodin in combination. This amounted to 1.38 per cent. by weight, or 1.69 gm. iodin per 100 c.c.

Potassium.—Weighed quantities of Iodum-Miller were evaporated on the hot plate until crystallization started, then concentrated sulphuric acid was added and as soon as the first evolution of iodin was over heat was carefully applied and the remaining organic matter destroyed and after addition of small amounts of ammonium carbonate the sulphate heated to constant weight. After this the sulphate was dissolved in water and an excess of platinic chlorid added. The solution was then evaporated nearly to dryness and the residue then washed with 80 per cent. alcohol, the washings being poured through a small filter. After the filter was thoroughly washed with the alcohol, a small hole was made in the bottom of the filter and any particles left were washed with water to the beaker containing the major part of the platinum compound insoluble in the alcohol. After all the platinum salt was dissolved, the solution was made acid with hydrochloric acid and small amounts of zinc added until the solution had become colorless and the platinum all precipitated as metallic platinum. By this method the following results were obtained: (*a*) 4.0318 gm. material yielded by ignition a residue weighing 0.0352 gm. or 0.87 per cent. and (*b*) 2.7006 gm. material yielded a residue of 0.0241 gm. or 0.89 per cent. As no sodium or ammonium was found, these residues represent practically potassium sulphate. Residue (*a*) in turn yielded 0.0332 gm. platinum, equivalent to 0.73 per cent. potassium sulphate or to 1.40 per cent. potassium iodid, which in turn is equivalent to 1.06 per cent. iodin. (*b*) This residue yielded 0.0252 gm. platinum, equivalent to 0.83 per cent. potassium sulphate, which is equivalent to 1.58 per cent. potassium iodid and to 1.21 per cent. iodin. The average of

potassium sulphate equivalents or 0.78 per cent. indicates that the residue left by ignition with sulphuric acid is potassium sulphate. The average of the weights of potassium sulphate by ignition, or 0.88 per cent., is equivalent to 1.28 gm. iodin, combined as potassium iodid, and agrees in general with the combined iodin found by difference, viz., 1.387.

From the foregoing it is concluded that Iodum-Miller is a glycerin solution of 1.68 per cent. iodin and 1.80 per cent. potassium iodid.

IOD-IZD-OIL (MILLER'S)

(Reprinted, with additions, from The Journal A. M. A., Oct. 2, 1915, p. 120)

Iod-Izd-Oil (Miller's) is said to be an "iodin combination" made "from the same Soluble Soot Iodin as in Iodum-Miller." It is said to "liberate Free Soluble Iodin" when applied to the skin, mucous surfaces, etc. It is further defined as "Soluble Iodin combined with water-white Hydrocarbon Oil" and is said to liberate "Soluble Iodin 2 per cent." While these statements suggest that Iod-Izd-Oil (Miller's) contains the iodin-potassium-iodid combination contained in Iodum-Miller, analysis indicated the oil to be a simple solution of iodin in liquid petrolatum. Quantitative determinations indicated, not 2 per cent. of iodin, as claimed, but only 0.42 per cent. and all of this was present as free iodin.

Details of Analysis

Iod-Izd-Oil is a violet-colored transparent oily liquid practically without odor but developing an iodin taste when placed in the mouth. When heated on the water bath the violet color gradually disappears, leaving a slightly yellow tinted oil, which has the general properties of liquid petrolatum or paraffin. Heating some of the oil until it is consumed leaves practically no residue, showing the absence of mineral constituents such as iodids. Shaking with water and evaporating the aqueous extract left no residue, showing absence of glycerin or soluble iodids. From these facts it is apparent that no "Iodum-Miller" could be present, as the latter contains both glycerin and iodids besides free iodin.

To determine the free iodin, weighed samples were diluted and then titrated with thiosulphate. By this method the following results were obtained: (*a*) 11.3531 gm. Iod-Izd-Oil required 3.91 c.c. tenth-normal thiosulphate, equivalent to 0.0492 gm. iodin, or 0.43 per cent. (*b*) 11.6896 gm. required 4.09 c.c. tenth-normal thiosulphate, equivalent to 0.0514 gm. iodin, or 0.44 per cent.

The total iodin was determined by fusing with sodium hydroxid according to the method of Kendall (*Jour. Biol. Chem.*, 1914, xix, 251).

Thus (*a*) 0.5364 gm. of the preparation required 1.07 c.c. tenth-normal thiosulphate, equivalent to 0.0134 gm. iodin, one sixth of which, or 0.41 per cent., represents the iodin of the preparation, and (*b*) 0.6162 gm. material required 1.31 c.c. tenth-normal thiosulphate, equivalent to 0.01649 gm. iodin, one sixth of which, or 0.44 per cent., represents the iodin of the preparation, making an average of 0.42 per cent. total iodin.

As the total iodin is equal to the free iodin, it is evident that the entire iodin content of the preparation is free, and that it is essentially a liquid petrolatum solution of iodin containing about 0.43 per cent. iodin. As the specific gravity of the preparation was found to be 0.832 at 25 C., the iodin content may be also expressed as 0.36 gm. per 100 c.c.

From the foregoing findings the statement that Iod-Izd-Oil Miller "liberates soluble iodin—2 per cent.," is untrue and is misleading.

HEXA-CO-SAL-IN

(Reprinted, with additions, from The Journal A. M. A., Oct. 2, 1915, p. 1203)

Of this preparation THE JOURNAL said:

"Hexa-co-sal-in (Hexa-Co-Sal-In Company, Red Bank, N. J.) is advertised as 'a condensation product of familiar composition.' The further explanation that it is 'colchi-magnesium salicylate with anhydrous hexamethylenamin' does not make this statement much clearer. 'Colchi-magnesium salicylate'—not to speak of its condensation product with hexamethylenamin—is unknown in chemical literature. As a matter of fact, an examination made by the Chemical Laboratory of the American Medical Association shows that Hexa-co-sal-in is a simple mechanical mixture of hexamethylenamin, magnesium salicylate and some colchicum preparation. The composition is therefore falsely stated.

"The preparation is advertised as:

"'Antirheumatic, Antineuritic, Urinary Antiseptic.'
"'Uric Acid Mobolizer' (sic).
"'Intestinal Antiseptic, Mildly Laxative.'
"'Whenever a salicylate is indicated use Hexa-co-sal-in.'

"The combination of salicylates, hexamethylenamin and colchicum in a routine formula is certainly inadvisable; where one of the ingredients is needed, the others may be

useless or even harmful. The unqualified advice to use hexamethylenamin and colchicum 'whenever a salicylate is indicated' is likely to do harm.

"The statement of the composition of this preparation is false; unwarranted therapeutic claims are made for it, and the mixture is unscientific. The Council held Hexa-co-sal-in ineligible for New and Nonofficial Remedies because of conflict with Rules, 1, 6 and 10."

Details of Analysis

Hexa-co-sal-in is a light brown finely granular powder having a faint odor resembling methyl amin. It is largely soluble in water, yielding a solution slightly acid to litmus. The aqueous solution, when treated with ferric chlorid, is colored violet, and when boiled with sulphuric acid, yields formaldehyd. After boiling with acid and making alkaline, the solution yields ammonia on boiling, indicating the presence of hexamethylenamin. This was further confirmed by the fact that the aqueous solution yielded a white precipitate with mercuric chlorid and an orange-colored precipitate with bromin water. The aqueous solution, when made alkaline with ammonia water and sodium phosphate added yields a precipitate of magnesium ammonium phosphate. These qualitative tests show the presence of a salicylate, hexamethylenamin, and magnesium.

To test for colchicum the hexamethylenamin was precipitated with mercuric chlorid, which did not precipitate the alkaloid. The filtrate was made alkaline and the precipitate which formed removed by filtration and the filtrate extracted with chloroform. The chloroform on evaporating left a residue which was soluble in water and alcohol, but not in ether. With acid the residue became yellow. With concentrated nitric acid a violet color was produced. This color is also given by solanin, but as there was no reason to expect the presence of this principle, the test was taken as confirmation of the claim that the preparation contained colchicum.

Microscopic comparison of the water insoluble portion with powdered colchicum seed indicated the identity of the colchicum.

The fact that hexamethylenamin could be extracted from the preparation with ether or chloroform showed that hexa-co-sal-in was not a chemical entity but a mechanical mixture.

ZEMO

(Abstracted from The Journal A. M. A., Oct. 16, 1915, p. 1387)

Zemo (E. W. Rose Medicine Company, St. Louis) is sold as "A Preparation for the Treatment of Eczema, Pimples, Dandruff and Similar Affections of the Skin and Scalp." While, in accordance with the requirements of the Food and Drugs Act, the manufacturer admits the presence of 35 per cent. alcohol in his product he gives no further information regarding its composition. Some of the claims that have been made for this preparation, through the medium of those newspapers that are willing to cater to this sort of business, are:

"There is nothing known that will stop itching like Zemo."
"It also cures dandruff, which is scalp eczema."
"Every form of Scalp Disease Cured Quick by Zemo."

An abstract of the chemists' report follows:

One original bottle of Zemo, manufactured by the E. W. Rose Medicine Co., St. Louis, was submitted to the Chemical Laboratory for examination. The bottle contained a brown fluorescent liquid, acid to litmus. The amount of alcohol was 28.35 per cent. absolute alcohol by volume. Alkaloids, heavy metals and iodids were not found. From the result of the tests made, it would appear that Zemo is a watery-alcoholic solution containing methylsalicylate, thymol, borax, tannic acid, glycerin, menthol and a phenol-like body.

THE JOURNAL concluded:

"Zemo stands exposed as a very ordinary mixture sold under misleading claims."

VARLEX COMPOUND

An Alleged Cure for the Liquor and Tobacco Habits

(Abstracted from The Journal A. M. A., Nov. 6, 1915, p. 1663)

"Varlex Compound," put on the market by the Varlex Manufacturing Company, Kansas City, Mo., is sold under the claim that it can be given secretly to "cure" the liquor and tobacco habits.

Varlex Compound is advertised by the "prescription fakes" method. Under the heading "Home Recipe for the Liquor Habit" the claim is made that a "well-known physician located in the Middle West, who has treated thousands of

cases of the liquor habit" gives the following "simple inexpensive prescription that can be given secretly in coffee, milk, water or in the food." The alleged prescription is:

Water	3 oz.
Muriate of Ammonia	20 grains
Varlex Compound	1 pkg.
Pepsin	10 grains

One package of "Varlex Compound for Making A Treatment For The Liquor And Tobacco Habit," prepared by Varlex Mfg. Co., Kansas City, Mo., was submitted to the Chemical Laboratory for examination. The package contained about 48 grains of a brownish-white powder, having a slightly sweet taste. Qualitative tests demonstrated the presence of milk sugar (lactose). Alkaloids and metallic substances were not found. Quantitative determinations indicated that the powder consisted of approximately 97 per cent. lactose and 3 per cent. moisture. In other words, it appeared to be essentially milk-sugar.

ALKALOL

(*Abstracted, with additions, from The Journal A. M. A., Nov. 6, 1915, p. 1665*)

Alkalol, manufactured by the Alkalol Company, Taunton, Mass., is sold as

"An alkaline antiseptic for mucous membranes. Agreeable, cleansing, nonirritant—used internally or externally."

It is advertised to be

". . . Particularly adapted to treating the membrane of the nose, mouth, throat, ear and eye, but can be used on any irritation or inflammation, or internally . . . is especially valuable in all forms of catarrh, acute cold in the head or hay fever and as an external application to burns, cuts, bruises, insect bites or itching conditions."

"Alkalol is more, infinitely more, than a simple alkaline solution."

"Appreciation of its peculiar physiologic action will explain why and how it is of surpassing effectiveness in all conditions where there is ulceration or perforations of the drug membrane."

Inquiries on the subject were received by THE JOURNAL and the Chemical Laboratory of the Association was requested to analyze a bottle of Alkalol purchased on the open market.

The Laboratory reported:

Alkalol was found to be a clear, light brown liquid with an aromatic odor and a saline taste, and having an alkaline reaction to litmus paper. Twenty-five c.c. of Alkalol evapo-

rated to dryness yielded a residue weighing 0.5027 gm., or about 2 per cent. The same amount of Alkalol titrated with tenth-normal acid, methyl orange indicator, required 31.97 c.c. equivalent to 0.2667 gm. sodium bicarbonate, or 1.06 per cent.

During the evaporation of Alkalol odors resembling eucalyptus, spearmint, cinnamon, etc., were noted. Finally only a vanilla like odor remained. In view of the statement made in some of the advertising literature that some of the constituents of Alkalol were balsamic in nature it is likely that a small amount of some substance like Siam benzoin, which has a vanilla-like odor, is present.

From the foregoing it was concluded that Alkalol is essentially a flavored, weakly alkaline solution containing small amounts of salicylate, benzoate and chlorate.

Details of Analysis

Twenty-five c.c. of Alkalol when acidified and extracted with chloroform and the latter evaporated yielded a residue weighing 0.0185 gm. The residue was partly crystalline and partly oily. The residue was taken up in ammonia water and shaken out with chloroform to remove substances of an oily nature, then made acid and again extracted with chloroform. The residue this time was crystalline in form. When treated with ferric chlorid solution a violet color was produced, indicating salicylate or some phenolic body. It further responded to the methyl salicylate test for salicylic acid. To test for benzoic acid the Mohler test (*Pharm. Zentralb.*, 1911, p. 217) was used. This consists in oxidizing the salicylic acid with potassium permanganate in alkaline solution, then making acid and shaking out with chloroform and evaporating the solvent. A small amount of residue remained which responded to the ferric chlorid test and the ethyl benzoate test for benzoic acid. Besides salicylic and benzoic acids there were evidences of the presence of a chlorate, for when the residue from evaporation of Alkalol is treated with sulphuric acid the substance becomes yellow and yields a chlorin-like odor. The presence of chlorate was further demonstrated by the Boettger test, viz., treating the substance with anilin sulphate and sulphuric acid. This test yielded the characteristic blue color given by chlorate under the same conditions. A small amount of sulphate was also found. Tests for heavy metals, such as arsenic, mercury, antimony, or copper, as well as potent drugs such as vegetable alkaloids, showed their absence.

DR. CHARLES FLESH FOOD

(Abstracted, with additions, from The Journal A. M. A., Nov. 13, 1915, p. 1747)

"Dr. Charles Flesh Food" is put out by the Dr. Charles Flesh Food Company, a concern that sells "toilet specialties," including such preparations as "Foot Relief" for "sore, tired, aching feet" and "Revivo" claimed to be a "Remedy for Dandruff and Scalp Diseases." "Dr. Charles Flesh Food" sold under such claims as:

"Applied to the skin nourishes by absorption."

"It builds firm, healthy flesh."

"Acts quickly and surely on a skin that is seamed and wrinkled either by exposure or age, smoothing away furrows of the forehead and lines about the eyes and mouth."

"Undeveloped busts and those shrunken through sickness or nursing may be materially increased in size; made full, firm, plump and rounded out into a beautiful contour by the use of this wonderful flesh developer. It acts alike on the growing girl and matured woman."

One box of "Dr. Charles Co. Flesh Food—Healing, Nourishing, Beautifying," was submitted to the chemical laboratory for examination. The box contained a pink-colored, highly perfumed ointment. When some of the ointment was rubbed on the skin, it was apparently absorbed. Qualitative tests demonstrated the presence of alcohol (small amount), petrolatum, corn starch, zinc (probably present both as zinc oxid and zinc stearate), a fatty acid, which on purification responded to tests for stearic acid (probably a mixture of stearic and palmitic acids), and a trace of magnesium. Bismuth, mercury, lead, galega, borate or phenol-like bodies were not found. Quantitative data were as follows:

The ointment was extracted in a Soxhlet apparatus with chloroform.

I. Solid residue (starch, zinc compound . . .) dried at 140 C.	42.5%
II. Chloroform extract (petrolatum, fatty acid . . .) dried at 100 C.	53.2%
III. Difference (water, volatile substance)	4.3%
	100.0

Residue (non-soluble in chloroform) (I):	
Starch (anhydrous)	89.8%
Zinc (as zinc oxid)	4.8%
Chloroform extract (II):	
Fatty acid	2.1%
Petrolatum (recovered)	94.0%

The ointment consists essentially of about 38.5 per cent. of starch (anhydrous), 51 per cent. of petrolatum, 2 per cent. zinc oxid and 1.5 per cent. of impure stearic acid, with perfume and coloring matter added.

THE JOURNAL commented on the findings as follows:

"From the report it is apparent that the alleged flesh food is no better than, if as good as, an ointment made by mixing five parts of vaseline with four parts of starch and adding a dab of zinc oxid. . . . The stuff is not, in any sense of the word, a 'flesh food'; it does not 'build firm healthy flesh,' it will not develop the bust and it does not 'nourish by absorption.'"

Details of Analysis

Extractives.—A sample of the ointment was carefully wrapped in two sheets of filter paper which had previously been percolated with chloroform, dried at 100 C. and weighed. Aluminum wire securely held the package together. The ointment was then extracted in a Soxhlet apparatus with chloroform. After the extraction was finished, the package containing the chloroform insoluble residue (I) was carefully opened, placed in a large weighing dish and dried for two hours in an electric oven at 140 C. The chloroform was removed from the contents of the flask, and the extract (II) dried for one hour in an electric oven at 100 C. (*a*) The weight of the sample was 3.3613 gm. The insoluble residue (I) weighed 1.4279 gm., and the extract (II) weighed 1.7816 gm. This is equivalent to 42.5 per cent. insoluble residue (I) and 53.0 per cent. of extract (II). (*b*) The weight of the sample was 3.3260 gm. The insoluble residue (I) weighed 1.4049 gm., and the extract weighed 1.7305 gm. This is equivalent to 42.5 per cent. insoluble residue (I) and 53.4 per cent. of extract (II).

Starch and Zinc.—The combined insoluble residues (I) were used for these determinations. 1.3467 gm. of the residue (I) was hydrolyzed with 70 c.c. of water containing 7 c.c. of hydrochloric acid. After cooling, the solution was filtered, by the aid of reduced pressure, through a Gooch filter into an Erlenmeyer flask. The contents were transferred to a 250 c.c. volumetric flask and with the washings made up to the mark.

Starch.—The hydrolyzed starch was determined in 25 c.c. of the solution above, according to the method of Allihn (Leach-Winton: "Food Inspection and Analysis," ed. 3, p. 608). The copper was determined electrolytically, allowing the current to pass through the solution over night using 12 milliamperes and 2.5 volts. (*a*) The weight of the copper was 0.2587 gm. This is equivalent to 89.8 per cent. starch. (*b*) The weight of the copper was 0.2610 gm. This is equivalent to 91.2 per cent.

Zinc.—The zinc was deposited electrolytically on a large nickel dish, the method being the same as that proposed for the U. S. P., No. IX, except that in place of a rotating anode,

a simple stationary anode was used and the current of 4.5 amperes and 5.2 volts allowed to run two hours instead of thirty minutes. (*a*) Fifty c.c. of the solution yielded 0.0102 gm. zinc. This is equivalent to 3.80 per cent. zinc. (*b*) One hundred c.c. of the solution yielded 0.0211 gm. of zinc. This is equivalent to 3.91 per cent. zinc.

Petrolatum and Fatty Acids.—A weighed portion of the chloroform extract (II) was transferred to a beaker, and dissolved in chloroform,[1] then transferred into an Erlenmeyer flask, and the chloroform removed by evaporation. About 1 gm. of anhydrous sodium carbonate[2] and 50 c.c. of alcohol was then added, and the contents allowed to slowly boil on the steam bath. After one half of the volume of the alcohol was thus removed, 50 or 60 c.c. of water was added, and the whole digested on the steam bath for four hours. The liquids were finally boiled over a Bunsen burner for a short time until the volume was about 30 c.c., and after cooling transferred to a separatory funnel, the flask being washed with both water and ligroin (40-60). The contents of the separatory funnel were shaken with two separate portions of ligroin and the ligroin solution washed with water. A small amount of chloroform was then added to the ligroin solution and the whole filtered through a plug of cotton. The ligroin was carefully evaporated on the steam bath, in a current of air. The residual extract was dried for thirty minutes in an electric oven at 100 C., and weighed as petrolatum. The aqueous solution (which had been shaken with ligroin) was acidified, allowed to stand one hour and then shaken with two separate portions of chloroform. The chloroform solution was washed with water, filtered through cotton and the chloroform evaporated in a weighed dish. The residue was dried at 100 C. (*a*) 1.8299 gm. of the extract (II) gave 1.6729 gm. of petrolatum[3] (ligroin extract) and 0.0332 gm. fatty acid. This is equivalent to 92 per cent. petrolatum and 1.82 per cent. fatty acid. (*b*) 1.3919 gm. of the extract (II) gave 1.3376 gm. of petrolatum (ligroin extract) and 0.0321 gm. of fatty acid. This is equivalent to 96 per cent. of petrolatum and 2.30 per cent. fatty acid. In these operations, a small amount of petrolatum was lost, so that the percentages given represent the amount *recovered*.

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1. This was done in order to facilitate the placing of the extract in the Erlenmeyer, and to remove all of the adhering substance from the spatula.

2. Sodium carbonate was used rather than the hydroxid. This because the extractions could be done much more readily.

3. The petrolatum was treated with both aqueous and alcoholic potassium hydroxid. The mixture was digested for six hours. After evaporation of the solvent, the residue was taken up in water, the petrolatum filtered off and the aqueous solution tested for a soap by acidifying with sulphuric acid. The solution remained clear after acidification; hence there were no fats in the extract.

LAXATIVE BROMO QUININE

(Abstracted, with additions, from The Journal A. M. A., Nov. 27, 1915, p. 1932)

"Laxative Bromo Quinine," which for years has been falsely advertised under the claim that it "Cures a Cold in One Day," is put on the market by the Paris Medicine Company, St. Louis. Apparently, the business was founded by one E. W. Grove, president of the concern, who is said to have amassed a fortune in the business.

In addition to Laxative Bromo Quinine, the Paris Medicine Company also puts on the market "Dr. Porter's Antiseptic Healing Oil," "Pazo's Pile Ointment" and "Grove's Pepsin Coffee." While Laxative Bromo Quinine is sold as a "headache remedy," "Grove's Pepsin Coffee" is sold under the claim that it is "the only harmless headache remedy"!

Some of the claims that have been, or are being made for Laxative Bromo Quinine are, in addition to the slogan already quoted:

"Cures Grippe—prevents Grippe."

". . . removes the cause of Colds, Coughs, Headache, Neuralgia, Grippe, Feverish and Malarious Conditions. . . ."

"The quinine that does not affect the head."

"Laxative Bromo Quinine will be found better than the ordinary quinine."

"Relieves a Cold in the Head in the shortest possible time."

"For Colds, Coughs, La Grippe, Bronchitis, Catarrh and Headache."

"AN IMPROVED QUININE, DOES NOT CAUSE NERVOUSNESS NOR RINGING IN THE HEAD."

The preparation was analyzed by the Chemical Laboratory, which reported:

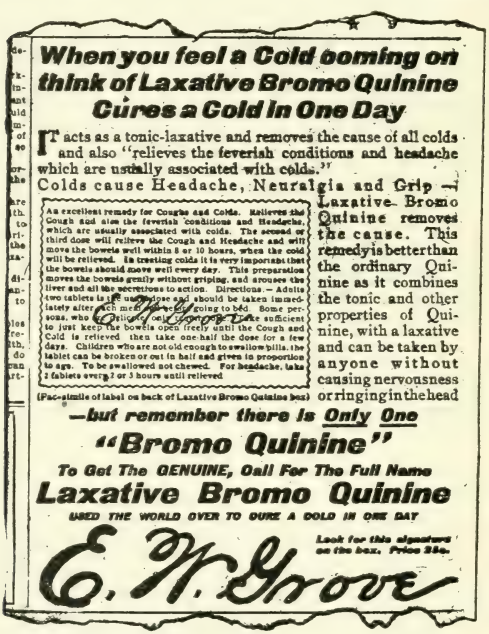
Laxative Bromo Quinine comes in the form of light brown tablets, possessing a faint characteristic odor and a bitter, rather sharp taste. Each tablet is stamped with the letters "L. B. Q." Qualitative tests showed the presence of aloin or aloes, quinin or cinchona alkaloids, phenacetin, caffein, starch, small quantities of chlorid and sulphate and a trace of bromid. Quantitatively, the tablets were found to have:

Phenacetin	44.78 per cent.
Caffein	4.33 per cent.
Quinin (or cinchona alkaloids)	8.91 per cent.
Starch	17.58 per cent.
Ash	5.00 per cent.
Bromid (Br^-)	0.51 per cent.
Chlorid (Cl^-)	0.40 per cent.
Sulphate ($SO_4=$)	0.20 per cent.
Aloin or aloes, and undetermined (by diff.)	18.29 per cent.

From the analysis it is concluded that Laxative Bromo Quinine is a mixture consisting mainly of phenacetin and aloin, with smaller quantities of caffein and quinin and only a trace of bromid.

Based on the foregoing, it appears that each tablet of Laxative Bromo Quinine (weighing 4½ grain) contains, as its essential ingredients:

Phenacetin (about)	2 grains
Caffein	½ grain
Quinin or cinchona alkaloids	2/5 grain
Aloin or aloes	Undetermined



Typical advertisement (from the Chicago *Daily News*) of Laxative Bromo Quinine.

In commenting on the analysis, THE JOURNAL said:

"While the name 'Bromo Quinine' naturally gives the impression that bromin and quinin are the important ingredients, analysis shows that the bromid content is only $\frac{1}{200}$ of the whole and corresponds to only about $\frac{1}{30}$ of a grain of potassium bromid or $\frac{1}{500}$ part of the pharmacopeial dose.

"The formula for Laxative Bromo Quinine Tablets, apparently, was changed about the time the federal Food and Drugs Act went into effect. At any rate, an analysis made for the American Medical Association in 1905 indicated that, in addition to the laxative principle, the tablets contained acetanilid, quinin sulphate and caffein. No trace of bromin was found at that time. An analysis made by the state chemists of North Dakota, and published in the Annual Report of the North Dakota Agricultural Experiment Station for 1907, also failed to disclose the presence of bromin. According to this report, when the North Dakota authorities notified the Paris Medicine Company of the results of their analysis, the company stated that previous to the enactment of the federal Food and Drugs Act 'they used the combined alkaloids of cinchona . . . as found in the cinchona bark, but were advised by the government to use some form of bromid in their preparation, and that they had since been using the bromid and quinin.' The North Dakota chemists were thereon furnished a sample of the 'new product,' which, 'on analysis showed the presence of a small amount of quinin and bromin.'

"The manufacturers of Laxative Bromo Quinine attempt to make the public believe that this product is 'an improved quinin' and 'better than the ordinary quinin' as well as 'the quinin that does not affect the head.' The real reason, of course, that Laxative Bromo Quinin Tablets do not affect the system in the same way as ordinary quinin is that there is practically no quinin present. While the average dose of alkaloidal quinin is 4 grains, the amount of this substance in Laxative Bromo Quinine is but $\frac{2}{5}$ of a grain. Put another way it means that, in order to get an ordinary pharmacopeial dose of quinin, it would be necessary to take ten Laxative Bromo Quinine tablets, and if this were done, the person taking it would get 20 grains of phenacetin, a dangerously poisonous dose.

"Again referring to the disparity between the composition of this preparation and the name, it is worth noting that one of the rulings, made by the officials who are intrusted with the enforcement of the federal Food and Drugs Act, declares that 'an article containing more than one . . . active medicinal agent is misbranded if named after a single constituent.' As the active medicinal agents in Laxative Bromo Quinine are not bromid or quinin but rather phenacetin and aloin, it seems strange that the company putting out this product has so far escaped prosecution under the federal law."

Details of Analysis

To prepare the material for analysis the contents of three boxes were powdered and thoroughly mixed. Before powdering, the tablets were counted and weighed. Each box was found to contain 24 tablets. These weighed: Box A, 6.4432; Box B, 6.7334, and Box C, 6.3790 gm. respectively, an average weight of 0.2714 gm. (4⅕ grains) per tablet.

The material was found to be partly soluble in water, forming a yellow colored solution with a very bitter taste, indicating aloes. The presence of aloes was further confirmed by the color of the solution becoming gradually red, and when heated with borax the solution took on a green fluorescence. A few grams of material was shaken with benzol, the solution filtered and the filtrate shaken with ammonia water. The appearance of a pink color in the ammonia water added further evidence of the presence of aloes.

Some of the material was treated with acidified water and then shaken with chloroform. The chloroform became yellowish green and on evaporation left a residue colored slightly green and possessing a bitter taste and also a very sharp taste like capsicum. The acid solution when made alkaline and shaken with chloroform and the latter evaporated yielded a residue which was brownish in color and bitter to the taste. It responded to tests for alkaloids and to the thalleoquin test for quinin. The presence of quinin or cinchona alkaloids, the statement on the label that the preparation contained phenacetin, together with the findings of analyses made some years ago, pointed to the methods of the Bureau of Chemistry for headache mixtures as the best means of separating and determining the constituents of this mixture (Bulletin 162 Bureau of Chemistry p. 200). Essentially the method consists in treating the mixture with acidified water and shaking the solution with chloroform, the latter taking out such substances as phenacetin or acetanilid and caffein if present, while other alkaloids would remain in the aqueous acid solution, from which they are eventually recovered by making alkaline and extracting with chloroform. The chloroformic solution suspected of containing caffein was evaporated to a small volume in presence of sulphuric acid which hydrolyzes the phenacetin to phenetidin sulphate, but leaves caffein intact. By shaking this acid solution with chloroform, caffein if present is removed. The phenetidin sulphate solution is treated with acetic anhydrid to reconvert to the acetylated derivative, phenacetin, and then extracting the latter with chloroform. By applying this method the various residues were obtained which responded to tests for quinin or cinchona alkaloids, caffein and acetphenetidin. A mixture of corn and potato starch was found also.

Quantitatively the following results were obtained:

Phenacetin.—(*a*) 1.2456 gm. material yielded 0.5540 gm. acetphenetidin, or 44.88 per cent.; (*b*) 1.1718 gm. material yielded 0.5238 gm. or 44.69 per cent. acetphenetidin, an average of 44.78 per cent. acetphenetidin or phenacetin.

Caffein.—(*a*) 1.1718 gm. material yielded 0.0497 gm. or 4.24 per cent. and (*b*) 0.9018 gm. material yielded 0.04 gm. or 4.43 per cent., an average of 4.33 per cent.

Quinin (or cinchona alkaloids).—(*a*) 1.178 gm. material yielded 0.1035 gm. or 8.83 per cent. and (*b*) 0.9018 gm. material yielded 0.0812 gm. or 9.00 per cent., an average of 8.91 per cent.

The various residues, although always containing more or less foreign coloring matter, were identified as follows:

Phenacetin.—The phenacetin residues were united and recrystallized once from hot water, the crystals dried on a clay plate and then in a desiccator and the melting point taken both alone and mixed with an equal amount of known phenacetin. In both cases the melting point was found to be 134-135 degrees, practically proving the identity of the substance as phenacetin. Further it responded to the pharmacopeial identity tests for phenacetin.

Caffein.—The caffein residues were rather deeply colored, and like the phenacetin residues were dissolved in hot water. The aqueous solution was then extracted with chloroform and the chloroform allowed to evaporate spontaneously, leaving a residue of silky needles characteristic of caffein. This residue further gave the murexid test and its acid solution yielded a precipitate with iodin solution but not with mercuric potassium iodid solution.

Quinin (or cinchona alkaloids).—The residues combined gave the thalleoquin test and the herepathite test and in dilute sulphuric acid gave a blue fluorescence. While the reactions are given by other cinchona alkaloids and since it has been stated that Laxative Bromo Quinine formerly contained the combined cinchona alkaloids, attempts were made to detect other cinchona alkaloids than quinin. A rough separation into ether-soluble alkaloids (quinin, quinidin and cinchonidin) and ether-insoluble (principally cinchonin) was made, but when these fractions were tested, it was found that each responded to the fluorescent test, showing that some quinin was present in each fraction and that either quinin was the sole alkaloid or that if all the cinchona alkaloids were present the separation was not complete. Attempts were then made to separate by the differences in solubilities of the salts of the alkaloids, but the quantities of "quinin residues" were too small to warrant further work along these

lines and so further attempts to determine whether or not the total cinchona alkaloids were present instead of quinin alone were not made.

Starch.—That portion which was insoluble in water and in alcohol was dried and weighed, then ignited and the ash weighed. The difference was taken as an approximate measure of the starch content, since all the ingredients found are soluble either in water or in alcohol. (*a*) 1.0989 gm. material yielded 0.2467 gm. or 22.45 per cent. substance insoluble in water or in alcohol. Ignition left a residue weighing 0.0543 gm. or 4.95 per cent. The difference, 17.50 per cent., is assumed to represent the starch content. (*b*) 0.9457 gm. material yielded 0.2131 gm. or 22.53 per cent. insoluble matter, which in turn left 0.0461 gm. or 4.87 per cent. ash. The difference, 17.58 per cent., makes an average of 17.58 per cent. for the starch content.

Ash.—Ash was determined by igniting to constant weight weighed portions of the powdered material. These determinations were made in addition to those above in the starch determinations because there was a possibility that the water extraction might remove some of the inorganic matter. 0.6228 gm. material yielded 0.0313 gm. or 5.02 per cent. ash, and 0.5446 gm. yielded 0.0271 gm. or 4.98 per cent. ash, an average of 5.00 per cent.

Sulphate (SO_4).—The material was fused with fusion mixture and sulphate determined as barium sulphate, thus: (*a*) 0.9707 gm. material yielded 0.0054 gm. barium sulphate or 0.22 per cent. sulphate (SO_4), and (*b*) 1.0200 gm. yielded 0.0045 gm. barium sulphate or 0.18 per cent. sulphate (SO_4), an average of 0.20 per cent. While this amount of sulphate could readily be ascribed to impurities in the various constituents of Laxative Bromo Quinine, it was calculated to quinin sulphate U. S. P. and found to represent 1.81 per cent. As the total quinin alkaloid content found amounted to 8.91 per cent., it is not probable that any of the quinin is present as the sulphate.

Halogens.—As the name of the preparation indicates the presence of bromin, tests were made for this substance. The absence of iodin was shown by fusing several grams of the materal with fusion mixture, acidifying the resulting mass with hydrochloric acid, adding ferric chlorid and shaking with chloroform. No trace of color could be detected in the chloroform, proving the absence of iodids.

Bromids.—To test for bromids in the possible presence of chlorids the method of Dechan (*Jour. Chem. Soc.*, 1886, L, 682; 1887, li, 690) was used. This depends on the fact that bromids are oxidized by potassium dichromate and sulphuric

acid in certain concentrations while the chlorids are not. In these tests 10 gm. dichromate were dissolved in 25 c.c. hot water and 1 c.c. sulphuric acid (1 part concentrated to 1 part water) added and then the bromid-containing solution. The latter was obtained by fusing some of the tablets material with fusing mixture and dissolving in dilute sulphuric acid. The combined solutions were heated in a high-necked Ladenburg distilling flask which was connected with a Peligot tube containing some potassium iodid solution and cooled by a cold water bath. The distilling flask was fitted with a rubber stopper through which a tube drawn to a capillary point passed extending into the solution. The free end of the Peligot tube was connected with an aspirator and a steady stream of air sucked through the apparatus during the operation. Before using the method it was tried qualitatively on a bromid solution of known strength and found suitable. When tried on Laxative Bromo Quinine the vapors distilled over were identified as bromin by the fact that they liberated iodin from iodid solution, colored alkaline anilin solution orange and colored fluorescein paper red, while the presence of bromid was thus definitely shown, the amount present, judged by the feebleness of the qualitative reactions, appeared to be small. To determine the quantity a differential silver determination was made. A measured amount of standard silver solution was added to a solution of the material after fusion with fusion mixture and acidification with nitric acid. The silver haloids (bromid plus chlorid) were filtered off and the excess of silver determined in the filtrate. From these figures the percentage of bromid can be determined in the following formula:

$$C \quad (26.81x) + 35.13\ (w-x)$$

In this C equals the number of cubic centimeters of fifth-normal silver nitrate used in precipitating the total haloids, w equals the weight of the total silver haloids, the figure 26.81 equals the number of cubic centimeters of fifth-normal silver nitrate equivalent to 1 gm. silver bromid, and 35.13 represents the number of cubic centimeters fifth-normal silver nitrate equivalent to 1 gm. silver chlorid; x equals the weight of silver bromid and w-x equals the weight of silver chlorid. Using this method the following results were obtained: 1.14942 gm. material yielded the following figures: Silver nitrate taken 24.93 c.c. fifth-normal. Weight of total silver haloids (w) equals 0.0410 gm. Weight of silver chlorid representing the excess of silver nitrate equals 0.0728 gm. which is equivalent to 23.62 c.c. fifth-normal silver nitrate, therefore the fifth-normal silver nitrate used equaled 1.31 c.c. Substituting these figures in the above equation:

$$1.31 - 26.81x + 35.13\ (0.0410-x)$$

x equals 0.0156 silver bromid or 0.0064 bromid or 0.43 per cent.

(*b*) 1.3913 gm. material yielded the following figures: Silver nitrate taken, 24.93 c.c. fifth-normal. Weight of total silver haloids equals 0.0403 gm. Weight of silver chlorid representing excess of silver used equaled 0.6746 gm. equivalent to 23.69 c.c. fifth-normal silver nitrate, indicating 1.24 c.c. used. Substituting the figures in the equations:

$$1.24 = 26.81x + 35.13\ (0.0403\text{-}x)$$

x equals 0.0204 gm. silver bromid equal to 0.0084 gm. bromin or 0.60 per cent., making an average of 0.51 per cent. bromin. This amount of bromin is equivalent to 2.64 per cent. quinin hydrobromid U. S. P. It is therefore impossible that all the quinin is present as the hydrobromid, but the result shows the probability of the presence of some of the quinin in the form of hydrobromid as suggested in the Eighteenth Annual Report of the North Dakota Agricultural Experiment Station, Part II, 1907, p. 140.

A summary of the analysis shows that Laxative Bromo Quinine contains the following:

	Per Cent.	Grams per Tablet[1]	Grains per Tablet[1]
Phenacetin	44.78	0.1215	1.8713
Caffein	4.33	0.0117	0.1709
Quinin (or cinchona alkaloids)	8.91	0.0242	0.3724
Starch	17.58	0.0477	0.7348
Ash	5.00	0.0135	0.2090
Bromid (Br')	0.51	0.0013	0.0203
Chlorid (Cl')	0.40	0.0011	0.0167
Sulphate (SO_4'')	0.20	0.0005	0.0083
Aloin and undetermined (by difference)	18.29	0.0596	0.92

1. Calculated on the basis of the weight of the average tablet viz.: 0.2714 gm. (4.17 grains).

DR. PIERCE'S PLEASANT PELLETS

(*Abstracted from The Journal A. M. A., Dec. 4, 1915, p. 2024*)

"Dr. Pierce's Pleasant Pellets" are made by the World's Dispensary Medical Association, Buffalo, the same concern that exploits "Pierce's Golden Medical Discovery," "Pierce's Favorite Prescription," "Pierce's Compound Extract of Smartweed," etc. Pierce's Pleasant Pellets are recommended to the public on the claim that:

"Being entirely vegetable in composition, these pellets operate without disturbance to the system, diet or occupation."

Elsewhere in the same advertising leaflet the public is warned against "harsh drastic pills, composed, as most of them are, of jalap, aloes, scammony, croton oil, gamboge and

elaterium"—all of them, it should be noted, products of the vegetable kingdom.

"Pierce's Pleasant Purgative Pellets" were examined in the Association's laboratory, and while no exhaustive work was done, the chemists reported:

"After removal of the coating, the inner pill responded to tests for emodin and aloin. Alkaloids, mercury or phenolphthalein were not found. Whether or not other emodin-bearing drugs besides aloin were present was not determined. Essentially, Pierce's Pleasant Purgative Pellets appear to be an ordinary laxative pill."

That the active principle of aloes was found in the pills is of interest in view of the fact, already referred to, that the leaflet advertising Pierce's Pleasant Pellets warns the public against the use of purgatives composed of aloes.

NOSE-IONS

(Abstracted, with additions, from The Journal A. M. A., Dec. 4, 1915, p. 2026)

Nose-Ions, made by the Nose-Ions Company, New York, was brought to the attention of the THE JOURNAL through numerous inquiries regarding its composition. These inquiries, together with the advertising matter sent in, were referred to the Chemical Laboratory, which reported:

The Nose-Ions circular matter referred to is a crude attempt to impose on a scientifically trained profession with pseudo-scientific patter about ions, ionic dissociation and the positive and negative charges of ions. The only intimation regarding the composition of Nose-Ions is found in a small circular wrapped around a sample package. Here it is stated that "Nose-Ions is composed of chemically pure Na-ions of sodium, chloride, Camphor and Menthol, combined with the base, Vaseline."

Were the matter deserving of scientific consideration it would be interesting to inquire just how the positive sodium ion was separated from the negative chlorin ion of sodium chlorid, and how the sodium ion was kept in the ionized condition while isolated. But since every positive ion exists, as such, only alone with a companion negative ion, such inquiry is superfluous.

A qualitative examination was made. From this examination it appears that Nose-Ions is essentially an ointment consisting of a petrolatum base containing some odorous principles such as camphor, menthol and eucalyptus with

some salicylic acid, and some quinin, probably in the form of sulphate. "Sodium ions," if present at all, are present in traces only.

Details of Analysis

Several sample packages of Nose-Ions were emptied of their contents and the contents thoroughly mixed. This mass was used for the analysis.

To test for sodium 3 or 4 gm. of the substance was decomposed with sulphuric acid and the acid driven off and the residue heated to redness. Scarcely a stain remained on the dish, and when tested by the flame test for sodium only the faintest reaction took place, indicating that only minute quantities of sodium could have been present. Further, some of the ointment was melted and then shaken out with hot water and the water extract tested. Again only very minute traces of sodium could be detected.

When the melted ointment was shaken with water it was noted that the aqueous part possessed a bluish fluorescence and a bitter taste, two properties indicating some quinin salt. The solution responded to the ordinary alkaloid tests and to the thalleoquin test for quinin. The aqueous solution was acid to litmus paper and responded only faintly to tests for halogens but responded rather strongly to test for sulphate. From these findings it is probable that the preparation in solution is quinin sulphate.

The aqueous solution also yielded a violet color with ferric chlorid solution, indicating some phenolic body. To determine the nature of this, the aqueous extract of Nose-Ions was made alkaline and the alkaloid extracted. The solution was then made acid and again extracted with chloroform. On evaporation the chloroform left a crystalline residue which in general had the appearance of salicylic acid. But the crystals appeared to be wet or sticky, so no melting point could be taken. The crystals were washed with petroleum ether and then dissolved in chloroform and several volumes of petroleum ether were added in the hopes of precipitating the pure body. No precipitation took place but on evaporating the liquid left clean crystals near the top edge of the vessel. These were collected, washed with petroleum ether and dried on a clay plate. The substance melted between 155 and 156 C. (uncorrected), which is practically the standard of the U. S. P. for salicylic acid. The crystals further complied with the U. S. P. test for salicylic acid.

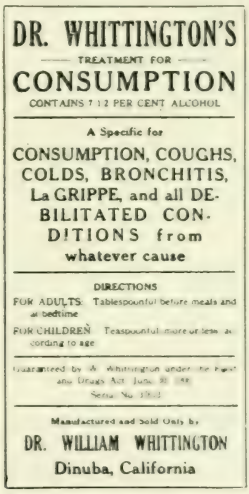
When subjected to steam distillation odors resembling camphor, menthol and eucalyptus were noted. The residue in the distillation flask had all the properties of white petrolatum.

DR. WHITTINGTON'S "SPECIFIC"

(Abstracted from The Journal A. M. A., Dec. 18, 1915, p. 2185)

"Dr. Whittington's Treatment for Consumption" is, according to the label, "manufactured and sold only by Dr. William Whittington, Dinuba, Cal."

One original bottle of "Dr. Whittington's Treatment for Consumption" was submitted to the A. M. A. Chemical Laboratory for examination. The bottle contained about 350 c.c. (12 fluid ounces) of a brown syrupy liquid. The liquid had an odor of raspberry and prunes and also somewhat vinous characteristics, with a tannin-like taste. The



Reduced photographic facsimile of the label on Whittington's "consumption cure." It obviously violates the federal Food and Drugs Act.

reaction toward litmus was acid. The specific gravity at 15.6 C. was 1.0963. The weight of ash from 100 c.c. was 0.73 grams. Qualitative tests indicated the presence of alcohol, magnesium, tannin and other vegetable acids, acetate, sugar, glycerin, and traces of calcium, potassium and sodium. tests for the following yielded negative results: heavy metals, haloids, sulphates, alkaloids, emodin-bearing drugs, benzoate, cinnamate, salicylate and glycyrrhiza. From this analysis it appears that "Dr. Whittington's Treatment for Consumption" is a flavored syrup, devoid of potent ingredients other than alcohol.

STUART'S CALCIUM WAFERS

(Reprinted, with additions, from The Journal A. M. A., Jan. 1, 1916, p. 51)

The following inquiry was received by THE JOURNAL:

"*To the Editor:*—Can you tell me the composition of a proprietary remedy known as Stuart's Calcium Wafers? I believe they are manufactured at Battle Creek. I am particularly interested to know whether there is any arsenic in this remedy C., Ann Arbor, Mich."

THE JOURNAL replied as follows:

"Stuart's Calcium Wafers are made by the F. A. Stuart Company, Marshall, Mich. The label of a specimen recently purchased on the open market reads: 'Stuart's Calcium Wafer Compound—For Constipation, Blood Disorders, Skin Affections, any Derangement of Blood, Bowels, Kidneys or Liver."

The specimen was examined in the Association's Laboratory. The chemist's report follows:

"Stuart's Calcium Wafer Compound consists of small brown coated tablets weighing on the average 0.0813 gm. (about 1¼ grains). The interior of the tablet is composed of an olive-colored material, which when moistened emits hydrogen sulphid. The material has a very bitter and unpleasant taste resembling aloes or aloin. Qualitative examination indicates that the 'wafers' consist essentially of calcium sulphid and aloes or aloin. No arsenic could be detected."

THE JOURNAL remarked in conclusion:

"Like other so-called 'blood purifiers,' Stuart's Calcium Wafers evidently are essentially cathartic."

Details of Analysis

The aqueous extract of the tablets when filtered and allowed to stand became reddish and when heated with borax developed a green fluorescence, indicating the presence of aloes. This test with the characteristic taste was considered sufficient to identify one of the ingredients of the tablets as aloes.

The acid extract of the tablets showed the presence of sulphid and responded to tests for calcium, indicating the presence of calcium sulphid. This was further indicated by the fact that the odor of hydrogen sulphid was apparent when the tablets were wet with water.

COLLOIDINE

(Abstracted, with additions, from The Journal A. M. A., March 11, 1916, p. 831)

Colloidine, manufactured by A. Dubois, Paris, France, and marketed in the United States by the Boracol Chemical Company, Passaic, N. J., is described as

"A Colloidal Vegetable Iodine Combination."

Colloidine is sold in the form of tablets said to contain each ⅛ grain of iodin combined with 1 grain of "Vegetable Albumen" obtained from gluten. The advertising says much of the colloidal state, which is "characteristic of living organisms," within which "the reactions are nearly always between colloids." It is asserted that:

"Colloidine acts not only like iodine, iodides, and all the derivatives of iodine in general, but by reason of its *Colloidal* or *'living state'* it possesses a specific action on a great number of diseases."

"3 tablets of COLLOIDINE are equivalent to 15 grains of iodide. . . ."

"The action of Colloidine is much gentler than that of all other products of Iodine. *Its elimination is slower, more regular and more prolonged.* . . ."

"Never produces Iodism."

At the request of the Council on Pharmacy and Chemistry, the Chemical Laboratory of the American Medical Association made a chemical examination of Colloidine. Its findings, in brief, were:

1. Iodin is present in Colloidine in the form of an iodid or a form which so readily yields iodid that the therapeutic effects of Colloidine administration would appear to be that of iodid medication. This is demonstrated by the fact that when Colloidine is treated with water all of the contained iodin goes into solution and from this aqueous solution silver nitrate solution precipitates all of the iodin.

2. Instead of the claimed iodin content of ⅓ grain (21.6 mg.) per tablet, the tablets of Colloidine were found to contain only 15.46 mg. (about ¼ grain) or about 72 per cent. of the amount claimed.

3. Each tablet corresponds in iodin content to $^{3}/_{10}$ grain potassium iodid or ¼ grain sodium iodid. The largest dose of Colloidine recommended—15 tablets per day in syphilis—corresponds to a dosage of 4½ grains potassium iodid, or 3¾ grain sodium iodid. The small dose of iodid administered evidently accounts for the reported absence of symptoms of iodism after the administration of Colloidine.

In commenting on the laboratory's findings, the Council said:

"Colloidine is called a

"'New Treatment of Rheumatism, Gout, Arteriosclerosis, Arthritis, Asthma, Emphysema, Scrofula and Syphilis.'

"Since the chemical examination shows that treatment with Colloidine must amount to the administration of iodid—nothing more—the following claims are unwarranted; they are even absurd.

"'Colloidine is the most useful medicine for Arteriosclerosis. It is not only a marvellous curative for this affection, but also an efficacious preventative in functional troubles of presclerosis . . .'

"'Colloidine facilitates and regulates the menstrual functions . . .'

"'Colloidine constitutes an ideal alterative for purifying the blood.'

"Finally, the recommendation to depend on Colloidine for the treatment of syphilis is fraught with danger."

Details of Analysis

The average weight of Colloidine tablets was found to be 0.3428 gm. Aqueous extracts of the powdered tablets responded to tests for iodids but showed no free iodin. Silver nitrate yielded a precipitate of silver iodid, and iodin could be obtained by shaking the solution with chloroform after oxidizing with ferric chlorid solution or hydrogen peroxid.

Quantitative iodin determinations were made, first, of the water-soluble iodid, by extracting the substance with water, liberating the iodin by means of ferric chlorid and extraction with chloroform, and titrating the chloroform solution with tenth-normal thiosulphate solution. Secondly, the total iodin was determined by fusion of the material with alkali, oxidizing the iodid formed to iodate by means of bromin, removal of the excess bromin by boiling, liberation of the iodin by addition of iodid and subsequent titration of the iodin with thiosulphate (Kendall's method, *Jour. Biol. Chem.*, 1914, xix, 251).

Using the first method, 0.6715 gm. material required 2.41 c.c. tenth-normal thiosulphate solution, equivalent to 0.03034 gm. or 4.51 per cent. iodin; and 0.7200 gm. material required 2.55 c.c. tenth-normal thiosulphate, representing 0.03218 gm. or 4.47 per cent., an average of 4.49 per cent. iodin.

By the second method, 0.9508 gm. material required 20.85 c.c. tenth-normal thiosulphate, equivalent to 0.04369 gm. or 4.59 per cent. iodin; and 0.9002 gm. material required 19.27 c.c. tenth-normal thiosulphate, equivalent to 0.0405 gm. or 4.50 per cent. iodin, an average of 4.54 per cent. iodin.

From the foregoing results it is clear that the water-soluble and total iodid are equal; in other words, the water extraction removes all the iodin present in the preparation.

As a confirmation test the aqueous extract of the tablets was treated with an excess of silver nitrate solution in nitric acid solution, the precipitate removed and the filtrate treated with hydrogen peroxid and tested for iodin by shaking with chloroform. No iodin could be detected. This is further evidence that all the iodin in Colloidine can be removed by water extraction. It also shows, as do the quantitative determinations reported above, that the total iodin content of Colloidine is present as an iodid or some form that yields iodid so readily as to react in every respect like iodid and therefore can be considered iodid as far as therapeutic use is concerned.

The average iodin content of Colloidine found by the two methods above outlined is 4.51 per cent. While the claimed iodin content is 1 grain (0.0648 gm.) in three tablets (1.0284 gm.), only 0.0464 gm. iodin was found in this quantity of Colloidine. This amounts to less than 72 per cent. of the claimed content.

From these figures it is evident that each tablet corresponds in iodin content to $\frac{3}{10}$ grain of potassium iodid or to ¼ grain sodium iodid. The largest dose recommended, 15 tablets per day, in syphilis, corresponds to a dosage of 4.5 grains of potassium iodid or 3.75 grains sodium iodid. The small dose of iodid thus administered evidently accounts for the reported absence of symptoms of iodism after administration of Colloidine.

The foregoing findings were submitted to the manufacturers of Colloidine by the Council on Pharmacy and Chemistry. In reply the methods employed were criticized and the following method given as the best procedure:

"Nine tablets are pulverized and heated with 20 c/c of a solution of silver nitrate $\frac{1}{10}$ in a beaker on the water bath. After ten minutes 5% of pure nitric acid are added and while keeping on heating on the water bath fuming nitric acid is added in portions of 4-5 drops at a time until effervescence has ceased.

"Under these conditions the formation of the well-known compound of silver iodid and nitrate of silver can sometimes be observed.

"Iodid of silver is also contained in solution in the acid liquor.

"By adding 100-150 c/c of water, the compound silver iodid-nitrate of silver is decomposed, and the iodid precipitated, and weighed as usual."

In trying to follow these directions it was noted that to add fuming nitric acid "until effervescence has ceased" would be an endless task, since effervescence continued as long as fuming nitric acid was added to the still hot solution. Thus no definite point could be determined at which to stop adding the acid. Two determinations made by this method varied by 100 per cent., while the duplicates and the average results of the two methods above reported agreed very satisfactorily, indicating that the firm's method is not reliable.

PART III

REPORTS NOT PREVIOUSLY PUBLISHED

ANALUTOS (CALCIUM ACETYL SALICYLATE)

At the present time, there are several trade names for calcium acetyl salicylate. In Germany there is Kalmopyrin. In Holland calcium acetyl salicylate is sold under the name "Analutos." A firm in England has designated this compound by the name "Soluble Aspirin." One of these products, Analutos and Analutos Tablets, was submitted to the Council on Pharmacy and Chemistry by the American representative for the Royal Pharmaceutical Works of Meppel, Holland. The referee of the Council in charge of the product requested the Chemical Laboratory of the American Medical Association to make an examination of the product submitted. The report was as follows:

Analutos is stated to be a soluble calcium salt of acetylsalicylic acid, having the formula $Ca[C_6H_4O(CH_3CO).COO]_2 + 2H_2O$. The specimen submitted was a white micro-crystalline powder, possessing a strong odor of acetic acid, and having a sour-sweet disagreeable taste. Analutos is claimed to be soluble one part in ten of water, producing a slightly acid solution. It is also claimed that a "watery solution is slightly colored red violet by strongly diluted Fe_2Cl_6."

It is stated that Analutos will yield from 13.00 to 13.50 per cent. of its weight as calcium oxid. Determination of the calcium oxid, made by ignition of Analutos powder, yielded (a) 13.95 per cent., (b) 13.89 per cent., (c) 13.95 per cent. Theoretically Analutos should yield 12.91 per cent. of calcium oxid.

In an approximate determination of the solubility of Analutos, 5 c.c. of a solution saturated at room temperature were found to contain 1.16 gm. of Analutos, indicating its solubility to be about 1 in 4.

In order to determine the decomposition of Analutos (already existing in the specimen or formed when dissolved in water) it was compared with aspirin and with a known control of sodium salicylate.

The method employed was to match the color produced by a definite amount of sodium salicylate and 1 c.c. of a 0.44 per cent. ferric chlorid solution, the whole having been diluted to 50 c.c. The method has previously been worked out in this laboratory and found to be satisfactory.

After making up the solutions, they were allowed to stand twenty-five minutes. The decomposition of Analutos (calculated from the amount of salicylate indicated by the color determination) was found to be 64.7 per cent. and 67.7 per cent. respectively. Aspirin, even in large amounts under exactly the same conditions gave no color whatever.

After the solution was heated to 55 C. and allowed to cool for one hour, the decomposition was found to be equivalent to 73.8 per cent. Under the same conditions aspirin gave only a slight coloration with 10 c.c.

When some of the dry powder was dropped onto a very dilute solution of ferric chlorid, a purple color was formed immediately. This demonstrated that salicylate was present in the dry powder to a relatively large extent. Aspirin gave no color reaction.

Details of Analysis

Calcium Oxid.—Calcium oxid was determined by igniting weighed portions of Analutos to constant weight. By this method the following results were obtained: (*a*) 1.0638 gm. Analutos yielded 0.1484 gm. or 13.95 per cent. calcium oxid (CaO); (*b*) 1.1086 gm. Analutos yielded 0.1667 gm. or 13.95 per cent. calcium oxid; (*c*) 1.0141 gm. Analutos yielded 0.1408 gm. or 13.89 per cent. calcium oxid. Average 13.92 per cent. Theoretically the calcium oxid content should be 12.91 per cent. (CaO).

Salicylic Acid.—One-tenth gram of sodium salicylate was dissolved in 1 liter of water. Each cubic centimeter therefore represents 0.0000863 gm. of salicylic acid. Two c.c. of this solution was added to 1 c.c. of ferric chlorid solution (0.44 per cent.) in 48 c.c. of water, and this taken as the 50 c.c. color standard.

Two-tenths gram of Analutos was dissolved in 500 c.c. of water, and allowed to stand twenty-five minutes. Some of the solution was then measured from a burette into a colorimeter tube (with contents as above) until the color matched the control.

Experiment A. 1.05 c.c. of Analutos matched 2 c.c. of standard sodium salicylate. 1.05 c.c. of 0.2 gm. of Analutos in 500 c.c. is equivalent to 2.10 c.c. of Analutos of 0.2 gm. in 1,000 c.c.

2.10 c.c. of Analutos is equivalent to 2 c.c. of sodium salicylate or to 2× .0000863 gm. salicylic acid.

1 c.c. of Analutos is equivalent to 0.0000822 gm. salicylic acid.

1 liter of Analutos is equivalent to 0.0822 gm. salicylic acid. Per cent. salicylic acid is equivalent to 41.10. Per cent. salicylic acid theoretical in Analutos is equivalent to 63.5 per cent. Decomposition is equivalent to 64.7 per cent.

Experiment B. One c.c. of Analutos matched 2 c.c. of standard sodium salicylate.

Calculated as above, the decomposition is equivalent to 67.7 per cent.

Aspirin, under exactly the same conditions and strength as Analutos, gave no color whatever, even with relatively large amounts.

Both solutions of Analutos and aspirin were placed on the steam bath, and the temperature allowed to rise to 55 C. They were then allowed to cool for forty-five minutes.

Experiment C. 0.92 c.c. of Analutos matched 2 c.c. of standard sodium salicylate. This corresponds to 67.7 per cent. decomposition.

With aspirin, only a slight coloration was given with 10 c.c.

Only about 10 per cent. degree of accuracy was aimed at.

A copy of the foregoing findings was sent to the manufacturers, whereupon the manufacturers, through their American agent, submitted some more specimens of Analutos. These specimens were also examined and found to have a much more agreeable taste, only a very slight odor, and not to respond to tests for free salicylate. The later specimens evidently were quite pure.

The Council, however, refused recognition to Analutos (THE JOURNAL A. M. A., Feb. 20, 1915, p. 684). In brief, the action was based on the following:

Analutos was stated to be the calcium salt of acetylsalicylic acid and to have the advantage over the latter of being more soluble and less liable to produce gastric disturbance. The evidence submitted did not show that Analutos had any great advantage over acetylsalicylic acid, or that it or its properties were discovered by the manufacturers. Since Analutos was thus shown to be an unessential modification of a well-known substance, without evidence of superiority or originality, the Council held that medicine should not be burdened with a new, arbitrary name which does not even indicate the relation to its well-known basic constituent.

DRYOXIDE

An inquiry was received in regard to the composition of Dryoxide, sold by the Dryoxide Chemical Company, Inc., New York. The specimen received was a powder contained in an envelope labeled "Oxygen Hydrogen Peroxide in Powder Form. Dryoxide." From the qualitative examination it appeared to be principally, if not entirely, sodium perborate. It responded to tests for sodium, borate, and peroxid, and had the general physical and chemical qualities of sodium perborate as described in New and Nonofficial Remedies.

MAYR'S WONDERFUL STOMACH REMEDY

Several years ago the laboratory reported[1] on this remedy. At that time "Mayr's Wonderful Stomach Remedy" consisted of a bottle of oil and two powders contained in a red carton.

The instructions directed the patient to take one powder at 3 o'clock in the afternoon; at bed-time the entire contents of the bottle (about a half-pint) was to be taken at one dose. The next morning the second powder was to be taken.

The bottle contained about six ounces of a bland yellow oil, which from the results of analysis appeared to be olive oil. The powders, each of which weighed about one ounce, appeared to be ordinary Rochelle salts, one disguised by the addition of about 6 per cent. compound licorice powder and the other by the addition of about 4 per cent. powdered licorice root.

Since the time of this early analysis the advertisements of this preparative had undergone some change, and hence in March, 1915, a specimen of Mayr's nostrum was examined in the Chemical Laboratory. The general appearance of this later product differed from that of the first specimen examined. The oil instead of being yellow was red and the character of the powders was changed. Tests indicated the following.

Powder 1	Rochelle and Epsom Salts.
Powder 2	Rochelle Salt.
Oil	Peanut or Olive, colored red.

1. The Journal A. M. A., Aug. 19, 1911, p. 671; Reports Chem. Lab., 1911, iv, 96.

It thus appears that the composition of this "patent medicine" has undergone a number of changes which, however, are unessential. Incidentally it may be observed that in the advertising matter the falsehoods are no longer directly stated but only implied.

ODO-RO-NO

Four original bottles of "Odo-ro-no," manufactured by the Odorono Company, Cincinnati, Ohio, were submitted to the Chemical Laboratory for examination.[1] The bottles contained about 1 fluidounce each of a rose-scented red liquid, which was acid to litmus paper. The specific gravity of the liquid at 15.6 C. was 1.1601. Qualitative tests demonstrated the following: aluminum, chlorid, sulphate, and a trace of zinc and iron (both ferrous and ferric forms). There were also indications of the presence of a benzoate-like body. Mercury, bromid, iodid, salicylate and alkaloids were not found.

Quantitative determinations yielded the following results:

Aluminum (Al^{+++})	3.45 per cent.
Chlorid (Cl^{-})	12.68 per cent.
Sulphate ($SO_4^{=}$)	0.51 per cent.

With phenolphthalein as an indicator, the acidity of the present specimens was nearly the same as that of the specimens examined previously. With Tropaeolin 00, however, the acidity of the present specimens was not quite so much as that of the older specimens, which indicates that there is not so much *free* acid.

From the examination, it is evident that the composition of "Odo-ro-no" is practically the same as previously.

Details of Analysis

After mixing the contents of the four bottles, 25 c.c. of the sample was diluted to 250 c.c. and aliquot parts taken for analysis.

Aluminum.—(*a*) Twenty-five c.c. yielded 0.1889 gm. of aluminum oxid (Al_2O_3), equivalent to 3.45 per cent. aluminum (Al^{+++}) in the original. (*b*) Twenty-five c.c. yielded 0.1889 gm. of aluminum oxid, equivalent to 3.45 per cent. aluminum in the original.

1. Report of a previous examination, together with the details of analysis may be found in the Annual Reports of the A. M. A. Chemical Laboratory, 1914, vii, p. 25.

Chlorid.—Chlorid was precipitated in the presence of nitric acid as silver chlorid. (*a*) Twenty-five c.c. yielded 1.4894 gm. of silver chlorid, equivalent to 12.69 per cent. chlorid (Cl^-) in the original. (*b*) Twenty-five c.c. yielded 1.4879 gm. silver chlorid, equivalent to 12.68 per cent. chlorid (Cl^-) in the original.

Sulphate.—(*a*) Twenty-five c.c. yielded 0.0362 gm. of barium sulphate, equivalent to 0.51 per cent. sulphate ($SO_4=$) in the original. (*b*) Ten c.c. of the original yielded 0.1436 gm. of barium sulphate, equivalent to 0.51 per cent. sulphate ($SO_4=$) in the original.

TOBACCO REDEEMER

One broken package of Tobacco Redeemer, manufactured by the Newell Pharmacal Company, St. Louis, was sent to the Chemical Laboratory for examination. The package contained two boxes. Qualitative tests indicated the following:

The larger box contained dark brown tablets bearing the letters "N.N." These tablets were quite bitter and the taste of licorice was very pronounced. A small amount of alkaloids were present but did not respond to tests for strychnin, quinin, caffein or mydriatic alkaloids. The tablets probably contain licorice and a bitter drug such as gentian as constituents.

The smaller box was labeled "Tonic Tablets." This box, as received, contained five tablets. These had a red coating easily removed by water, and also a covering of calcium carbonate, inside of which was a brown mass very bitter in taste. This inner substance responded to tests for aloes or other emodin-bearing drug and strychnin. Owing to the limited amount of material other tests were not made.

VITAZONE

"Vitazone" is stated to be "Produced by Vitazone Remedies Co., Nashville, Tenn." A correspondent advises that Vitazone was formerly sold under the names "Acid Iron Mineral" and "Acid Iron Earth," and was being exploited especially in the South.

From a circular which accompanies the trade package we learn that:

"Vitazone is a concentrated liquid mineral leached from a stratum of mineral earth located near Bladen Springs, Ala."

"In the preparation of Vitazone no alcohol or drugs of any kind are used. The mineral is taken from the earth, placed under shelter until it dries and slacks [slakes], then it is put into hoppers and pure spring water poured over it. The 'Drip' is what we call Vitazone."

"The medicinal properties are compounded in mother earth and no chemist has yet been able to produce a like article."

"The curative properties are phenomenal in such diseases as indigestion, dyspepsia, constipation, dysentery, rheumatism, eczema, tetter, ringworm, catarrh, diseases of women, fresh cuts, old sores, colic, kidney, liver and bladder disorders, piles, burns, general debility, and as a tonic for old people it has no superior, if an equal."

It is further recommended for sore eyes, pellagra, sore throat, teething children and as a blood purifier.

The laboratory found Vitazone to be a brown liquid having an astringent and metallic taste and an acid reaction toward litmus. The preparation contained a small amount of sediment. Qualitatively, phosphates, nitrates or heavy metals such as silver, mercury, bismuth or lead could not be found. A trace of chlorid was present. The liquid contained relatively large amounts of sulphate and of iron, in both the ferrous and ferric state. A small amount of some organic matter was present—probably sugar.

The total iron content was found to be equivalent to about 1 per cent. ferric oxid, which corresponds to 4 per cent. crystallized ferrous sulphate ($FeSO_4+7H_2O$) the form in which the iron is probably largely present.

It is concluded that Vitazone is essentially an aqueous solution of ferrous sulphate, with some ferric sulphate.

This preparation does not differ greatly from some of the pellagra "cures" that have been exploited in recent years in that iron is the essential constituent.

WHICHER'S RHEUMATIC REMEDY

The aid of the Association's chemical laboratory was invoked to find out if "Whicher's Rheumatic Remedy" contained the essential constituents of most "Rheumatic Remedies," namely, *iodides* and *salicylates*. Both of these substances were found to be present in relatively large proportions.

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